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Archives of Neurology and Psychiatry

VOLUME 15 MAY, 1926 NUMBER 5

SENSORY DISTURBANCES IN MULTIPLE SCLEROSIS

THEIR SIGNIFICANCE IN DIAGNOSIS *

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PRAGUE, CZECHOSLOVAKIA

It has long been known that sensory disturbances are of frequent occurrence in multiple sclerosis. The honor of having first called attention to this fact belongs to Oppenheim and C. S. Freund. Nevertheless, the fact does not seem to have become generally known among physicians, and it is still frequently stated that absence of sensory disturbances is characteristic in multiple sclerosis. This contradiction is explained by the fact that, as a rule, severe, persistent disturbances of sensibility, such as occur, for example, in transverse myelitis, are absent. But transient, fugitive paresthesias are very frequent, and there are few cases in which, if careful inquiry is made, the patient will not report them.

I have previously called attention to the significance of sensory disturbances in multiple sclerosis, and the more closely I have studied my patients, the more frequently I have found such disturbances. The clinical diagnosis of multiple sclerosis is often so difficult that I feel assured a new symptom will not be unwelcome. Many further observations by others are necessary before a definite judgment can be formed as to the diagnostic value of this symptom, and my main purpose is to call attention to the need for further study of the question.

The clinical course and final outcome of multiple sclerosis are characteristic, but there is no single pathognomonic symptom. Taken collectively, however, temporal pallor of the optic disks, nystagmus, absence of abdominal reflexes, intention tremor, scanning or dragging speech, attacks of uncontrollable laughter, palsies of the ocular muscles and central scotoma may be considered characteristic. The age of the patient is also important, since multiple sclerosis usually has its onset in youth. Occasionally, however, it begins at a more advanced age, as in a patient observed by me, who developed a left sided hemiparesis at the age of 65, and in whom necropsy revealed the lesions of this disease.

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The following case reports from my own experience have been selected from a larger group, and are intended to illustrate certain recurring types.

REPORT OF CASES

Cases in Which the Diagnosis of Multiple Sclerosis Seemed Certain

CASE 1.—A youth, aged 18, who had suffered from headache for three months, complained that the right leg became easily fatigued, and would then drag, and also of anesthesia in the right hand and right leg. Previously there had been loss of sensation in the entire left half of the body, with the exception of the head; after any excitement, the anesthesia had extended to the right side. For two years past, speech had been slower and lower pitched.

Physical examination revealed slow speech, bilateral absence of the abdominal reflexes, ataxia of the right arm and right leg, hypesthesia of the entire right half of the body, anesthesia of the entire palmar and dorsal surfaces of the third, fourth and fifth fingers, disturbance of the sense of position in the right foot and right hand and change in stereognosis. At this examination, eye disturbances, nystagmus and the Babinski reflex were absent. On a second examination, a Babinski sign was present in the right foot, and nystagmus was observed on looking to the left. The right fifth and fourth fingers, and the ulnar side of the third finger gave evidence of hypesthesia.

CASE 2.—A youth, aged 19, stated that his affection began with tinnitus, which was more marked in the left ear. About ten months later, the patient on awaking one morning was unable to speak, had a feeling of weakness in his right hand and could not move his tongue to the right. A few weeks later, paresthesia developed in the terminal phalanges of the third and fourth fingers of the right hand. A month later, the patient complained of a feeling of rigidity in the fifth finger of the left hand, and, in another month, of paresthesia in the fifth finger of both hands and also in the adjacent ulnar region as far as the wrist.

Examination revealed only bilateral nystagmus. In the beginning, following the sudden onset, an articulatory disturbance of speech and a right-sided facial paresis were observed, but they disappeared later. The blood Wassermann test was negative.

CASE 3.—The first symptom in this patient, a young man, was impaired vision (objects appearing dim and cloudy), involving first the left and then the right eye. Five months later, the gait became affected. Previously, anesthesia had been present in the right arm from the fingers to the elbow. The patient stated that he occasionally experienced a "shooting" hot flash extending from the fingers to the shoulder on the left.

Examination of the left eye revealed pallor of the whole optic disk; in the right eye the upper and nasal portions of the disk were pale, and the edges were indistinct. Nystagmus was present in all directions. The right corner of the mouth was weaker than the left. The patellar reflexes were exaggerated. Ankle clonus and a positive Babinski sign were present on both sides. Abdominal and cremasteric reflexes were absent. Romberg's sign was present, and ataxia was noted in both legs. There were no disturbances of sensibility.

CASE 4.—A man, aged 31, in 1914, began to experience violent sciatica-like pains in the left leg, extending from the trochanter to below the popliteal fossa. In December, 1922, the patient observed that he occasionally dragged his left foot, especially in walking uphill. The leg felt "dead."

Examination, Nov. 4, 1923, revealed: bilateral absence of abdominal and cremasteric reflexes, with positive Babinski and Rossolimo signs; ankle clonus in the left foot; positive Romberg sign; ataxia of the legs, especially the left; paresis of the left leg. Sense of movement in the toes of the left foot was disturbed; otherwise, sensibility was intact. There were no disturbance of vision, no diplopia and no nystagmus; the ocular fundi were normal. The condition in September, 1924, was as follows: the paresis of the left leg, which had earlier improved as the result of heat applications, had returned; weakness was present in the right arm; there was a feeling of numbness in the radial half of the right hand and forearm to the elbow, and in the first, second and half of the third finger. For a time, vision in the left eye had been lost, but the objective eye findings were normal at this time. The patient evidently had had a central scotoma of the left eye, which soon disappeared.

Case 5.—A woman, aged 50, stated that since October, 1922, she had been unable to walk, her legs had been stiff and hard to manage; she had had a feeling of contusion in the hands, and the second finger often and the other fingers occasionally seemed "dead." The right hand was worse than the left, but the left leg was worse than the right. Vision was impaired. Since June, 1922, urination had been difficult.

At the age of 21, she had had a right-sided facial paralysis, together with vomiting and dizziness. Then, for fifteen years there was a complete remission; this was followed by a condition resembling, but less severe than, the present, which lasted for three months. There was then a second remission extending over a period of sixteen years.

Examination, Nov. 24, 1922, revealed paresis of the right facial nerve affecting all three branches, and hypesthesia and hypalgesia of the right half of the face. Babinski and Oppenheim signs were positive on both sides; ankle clonus was present on the left; the Romberg sign was positive (sensation of falling to the right); the gait was spastic, and the finger-nose test revealed ataxia and tremor. There was bilateral atrophy of the optic nerve. Sensibility was intact. The Wassermann test in blood and spinal fluid was negative, even with the graduated method; the fluid contained fourteen cells, Nonne-Apelt and Pandy tests were weakly positive, and the hemolysin test was negative.

Case 6.—A man, aged 25, about April, 1922, had suffered from dizziness, and about six months later noted weakening of vision (clouding) in the left eye and later diplopia. There was a disturbance of deglutition and of speech. A dead, numb feeling was noticed in the right half of the face from the upper lip to the hair line; the chin was not affected. After two weeks the numbness passed away, but soon appeared in the left leg, first in the sole of the foot; it then traveled upward to the face. Weakness in the legs was complained of; during urination the patient was obliged to strain, and impotence was present.

Examination, April 24, 1924, revealed: nystagmus, especially to the left; bilateral ptosis, more marked in the left eye; paralysis of the right abducens nerve; atrophy of the left optic nerve; in the right eye, central scotoma for all colors; abdominal and cremasteric reflexes absent; Babinski reflex positive bilaterally; ataxia of the left arm and leg; Romberg sign positive; speech slow; sensibility in the left half of the body reduced, and sense of movement in the toes of the left foot disturbed.

Case 7.—A man, aged 23, had "meningitis" in 1917, with diplopia, vomiting, no fever and left-sided hemiplegia in which the face was involved. Formication was continuously present from the left great toe up to the head. There was a slight cloud before the left eye. The patient then improved, so that he could again

attend to his work. In the preceding week, there had been a sudden deterioration of vision of the left eye; the left arm and leg had become weak, and urination had been difficult.

Examination, Feb. 26, 1923, revealed: nystagmus; motor weakness in the left arm and leg; ataxia and intention tremor in the left arm; the Romberg sign sometimes positive and sometimes negative. Sensibility in the whole left side of the body was reduced. On both sides, the patellar reflexes were accentuated, the Babinski sign was positive, and the abdominal reflexes were very weak.

Case 8.—A man, aged 24, had noted for eighteen months a weakening of vision in the left eye. Examination, Oct. 20, 1922, revealed: bilateral neuritic atrophy of the optic nerves; central scotoma in the left eye for all colors; nystagmus; left arm and leg weaker than the right, and abdominal reflex weaker on the left than on the right. The Romberg sign fluctuated. Sensibility to pain in the entire left side of the body was reduced. Sense of movement in the left leg was impaired.

Case 9.—An unmarried woman, aged 26, in September, 1922, suffered from dizziness, vomiting and diplopia. For a time, the condition improved; but in February, 1923, the patient could not walk. She could not advance the left leg; and the left leg and the left hand trembled. The left side was weaker than the right. Occasional attacks of formication and numbness occurred. These began in the right temple, passed across the neck and shoulder, and extended to the ends of the fingers; thence over the trunk and down into the feet.

Examination, Oct. 23, 1923, revealed: nystagmus on looking to the right; left patellar reflex more marked than the right; abdominal reflexes absent bilaterally. Ankle clonus was noted in the left foot. The Babinski and Oppenheim signs were positive on both sides. There was a slight intention tremor. The Romberg sign fluctuated. There was a bilateral temporal pallor of the optic disks. The blood Wassermann test was negative.

Case 10.—A man, aged 34, who had suffered for ten weeks from dizziness and headache, complained that he could not speak easily and freely—he would have to stop in the midst of a sentence; after sitting for a while it was difficult for him to walk; for some time he had had no feeling in the left side. The blood Wassermann test was negative.

Examination, Nov. 16, 1923, revealed: paresis of the right abducens nerve; nystagmus; slight right facial weakness; deviation of the tongue on protrusion to the left; tendon reflexes exaggerated; abdominal reflex absent on the left, though the upper reflex could be elicited on the right; cremasteric reflexes absent; bilateral ankle clonus and Babinski sign. Sensibility: Beneath the costal arch there was a girdle of hyperesthesia; below that zone, hypesthesia, somewhat more marked on the right than on the left, was noted.

Case 11.—An unmarried woman, aged 21, stated that her sickness had begun eighteen months previously with rheumatism and stabbing pains in the region of the heart. The pain spread over the whole thorax, and there were severe pains in the shoulders. For several months past, the patient had found it difficult to walk. In recent weeks, there had been at times a cloud before her eyes; after reading for some time diplopia would be noted. During the last year, she had had shooting pains between the thumb and first finger of the right hand; also pains in the outer side of the left thumb. For a time, urination was difficult.

There was bilateral temporal pallor of the optic disks, and nystagmus. The patellar reflexes were exaggerated. The abdominal reflexes were absent, and the Babinski sign was positive on both sides. The Romberg sign was positive. Ataxia and intention tremor were observed on the left.

CASE 12.—A man, aged 36, had presented, in 1922, retrobulbar neuritis and temporal pallor of the optic papillae (Professor Löwenstein). In March, 1925, there was an unpleasant feeling in the right shoulder. Later, influenza developed, after which the pains in the right shoulder became worse, and during the following days extremely severe.

Examination, April 7, 1925, revealed: pupils equal, not dilated, not round, but reacting normally; eye movements normal, no nystagmus. The facial nerve, the tongue, and the trigeminus presented no peculiarities. The right optic papilla was pale throughout; the left showed temporal pallor. The left abdominal reflex was weaker than the right; both could be exhausted. The cremasteric reflex was absent on the right, present on the left. The patellar reflexes were present; the achilles reflexes were weak; the plantar reflex on the right was often of extensor type. Motility and sensibility were normal. After about three weeks, the pains gradually diminished; but paresthesias in the right hand and especially in the second finger, remained.

Cases in Which the Diagnosis Is Only Probable

CASE 13.—A woman, aged 49, had presented in 1908 weakness of the left arm, with numbness in the first and second fingers; and, since 1919, weakness and stiffness of the left leg. Retention of the urine was difficult and constipation was somewhat in evidence.

Examination, April 5, 1923, revealed: paresis of the left leg, with dragging of the left foot in walking; spasticity of the left leg; patellar reflexes exaggerated, and Babinski sign positive bilaterally. In November, 1923, possibly owing to a fall, severe pains appeared in the outer side of the left upper arm and were referred to as "creeping." The pains came on especially when the patient was walking.

The left optic papilla appeared, on the whole, to be paler than the right (Dr. Asher). The diagnosis in this case was uncertain, though the remittent course, the absence of abdominal reflexes, and the eye findings pointed to multiple sclerosis.

CASE 14.—A woman, aged 52, who for the last three years had dragged the left foot in walking and experienced sharp pains in the right leg, complained that the second finger of the left hand had felt as if asleep for the last six weeks.

Examination, Sept. 6, 1923, revealed: patellar reflexes exaggerated, especially on the left; ankle clonus and Babinski sign on the left; spastic paresis of the left leg; left abdominal reflex absent. In the left eye, the temporal portion of the disk was paler than the nasal part. The blood Wassermann test was negative.

COMMENTS

In the cases described, it is possible to distinguish several varieties of sensory disturbance.

Subjective Disturbances.—Abnormal sensations or paresthesias—numbness, tingling, formication, a feeling of numbness or "going to sleep"—are very frequent. They are mentioned in twelve of the fourteen cases and are absent only in Cases 8 and 11. The distribution of the paresthesia shows differences which seem to constitute certain characteristic groups.

In Cases 1, 6 and 10, one half of the body, with or without inclusion of the face, have been numb. The paresthesias were all transient, their

duration ranging from a few days to a few weeks. The fluctuating character of the symptom is especially striking; a sense of numbness on one side of the body might disappear only to develop on the other side. In Case 1, for example, the left half of the body had felt numb for a time; then, after any excitement, the numbness appeared on the right side. Similarly, in Case 6, a "wooden, dead feeling" was experienced in the right half of the face, though the chin escaped (first and second branches of the trigeminus only); this was followed by numbness in the left half of the body which began in the sole of the foot and gradually extended in the course of several days up to the face. Often the complaint is of formication in one half of the body; this may persist for some time, as in Case 7, or occur episodically in a form resembling sensory jacksonian attacks, as in Case 9.

In a second group, the paresthesias affect one limb or a part of one limb; in Case 3, the right arm; in Cases 5 and 10, the whole hand; in Case 6, the right half of the face.

Considerable interest attaches to the third group in which there is involvement of individual fingers corresponding to the so-called segmental sensory distribution (preaxial and postaxial types of Head). In Case 2, the patient complained of "going to sleep" of the third and fourth and later of the fifth finger; then in the fifth finger of both hands and in the ulnar side of both hands. In Case 4, there was transient numbness in the radial half of the right hand and forearm, and in the first, second, and half of the third finger. In Case 13, there was numbness in the first and second fingers of the left hand. In Cases 5 and 14, the second finger alone was affected.

These facts demonstrate the frequency of these fugitive, transient and constantly changing paresthesias in multiple sclerosis. I am inclined to attribute to them considerable diagnostic value, but further research in this direction is needed. I have purposely included in my series of cases some in which the diagnosis is established beyond question by the presence of such symptoms as temporal pallor of the optic disks, nystagmus and loss of abdominal reflexes, as well as others in which the diagnosis was less certain. Special attention may be called to Cases 5 and 9, in which the diagnosis is unquestionable. Since paresthesias are to be observed in such cases as these, it seems to me justifiable to regard these symptoms as corroborative evidence for the diagnosis of multiple sclerosis in more doubtful cases, such as Cases 13 and 14. In estimating the frequency and diagnostic value of paresthesia, patients must be questioned closely and often directly concerning its occurrence, as they often attach no importance to it and may even have forgotten that it had been present because of its short duration and remote occurrence. The more closely I have questioned my patients for

a history of paresthesia, the more frequently I have found it, and I am convinced that there is scarcely a case of multiple sclerosis in which this symptom is lacking.

Pains.—Though comparatively rare in multiple sclerosis, pain is sometimes complained of. Concerning this, Oppenheim states in his textbook: "Patients complain occasionally of stabbing, piercing and twingelike pains in the extremities, the joints or the intercostal region. These pains, however, are seldom sufficiently severe to occupy the foreground of the picture and almost never take on a lancinating character. In exceptional cases they may become so intense as to justify the term 'neuralgia.'" In one case Oppenheim observed trigeminal neuralgia, and at necropsy a sclerotic focus was found at the point of exit of the trigeminal nerve.

In my series, pains—sometimes severe—occurred in four cases. In Case 4, indeed, the affection began with a left-sided sciatica, which was followed by spastic paresis of the left leg. The progress of the affection, the transient central scotoma, the paresthesias, the age of the patient and the remissions make the diagnosis of multiple sclerosis practically certain. In Case 11, in which the diagnosis is undoubtedly correct, the pains were prominent. The affection began with a stabbing pain in the region of the heart, which extended gradually to the whole side of the thorax; then, exceedingly severe pains developed in the shoulders. Of special interest is a second area of pain between the thumb and first finger of the right hand and in the outer side of the left thumb. In Case 12, the patient had unusually severe neuralgic pains in the right shoulder; after these subsided, paresthesias remained in the fingers of the right hand. Case 13 is worthy of note in that not until late in the course of the disease did severe pains appear in the outer area of the left forearm; they were intermittent and were elicited more particularly by walking. In this case the nature of the pains suggested a tumor of the spinal cord, but the long nonprogressive, more intermittent course and the transient episodic appearance of the pains were opposed to such a diagnosis.

Objective Disturbances.—It is possible to distinguish various groups also of objective disturbances in sensibility. The reduction may be limited to one side of the body, as in Cases 1, 6 and 7. In Case 8, in which no subjective sensory disturbances were reported, there was reduction of objective sensibility in the whole left half of the body.

In some of the cases reported, changes in sensibility of segmental distribution were found; for example, in Case 1, there was anesthesia of the palm of the hand and of the third, fourth and fifth fingers. Of special interest, because evidently of rare occurrence, was the disturbance in sensibility in Case 10—a girdle of hyperesthesia below the costal

arch. This points to root involvement. In Case 5 hypesthesia and hypalgesia were noted in the right half of the face.

Attention may also be called to the disturbances in the sense of movement and position in Cases 1, 4, 6 and 8. In Case 1, the stereognostic sense was disturbed.

SUMMARY AND CONCLUSIONS

1. Not only are disturbances of sensibility of various kinds in multiple sclerosis frequent, but it appears that there is scarcely a case in which they do not occur.

2. Fugitive, rapidly shifting paresthesias are characteristic symptoms in multiple sclerosis which appear to have a high diagnostic value. Often the paresthesias shift from one side of the body to the other.

3. The paresthesias may be divided into various groups on the basis of distribution. They may affect all of one side of the body or be confined to certain parts (face, arm, hand, one or more fingers); or they may present a segmental distribution (preaxial or postaxial type).

4. In one case, paresthesias were described which affected one side of the body and resembled sensory jacksonian attacks.

5. Objective disturbances of sensibility are frequent. They may appear on one side of the body—hemihypesthesia or hemihypalgesia; they may involve separate parts of the body, such as the face, or they may have a segmental distribution.

6. Not infrequently, disturbances of sense of movement were observed in the toes. In one case astereognosis was present.

7. In one case a girdle of hyperalgesia was noted on the trunk.

8. Pains in multiple sclerosis are rare and seldom dominate the clinical picture. However, in four cases of the series reported, severe pains were manifest from time to time. In one, the disease began with sciatica on one side; in another, during the later course of the disease, severe pains appeared in an upper arm; in a third case, the disease began with severe rheumatoid pains in one side of the thorax and in the shoulders (in that case there were also circumscribed pains between the thumb and first finger of one hand and in the outer side of the other thumb); in one case neuralgia-like pains were felt in the shoulder.

THE DEVELOPMENT OF THE MENINGES*

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The meninges engage a constantly increasing attention from those interested in the diseases of the nervous system. The origin and flow of the cerebrospinal fluid and the congenital and inflammatory adhesions leading to interference with its circulation are of the greatest importance. No less so are the diverse neoplasms which take origin from or are associated with these structures. For the intelligent interpretation of their pathology it is necessary to have not only knowledge of the morphology of the meninges but also a clear understanding of their developmental background. Yet, as Weed [1] has said, "Probably no field in embryology has been less explored than that relating to the meninges." A reference to any of the standard textbooks on embryology reveals little but a condensation of the opinions of His and Kölliker, and the literature of recent years contains no notable contribution to this subject aside from that of Weed.

LITERATURE

It was assumed by the early investigators who first recognized the primary division of the blastoderm into layers, that all the structures of the nervous system including its enveloping membranes arose from the infolding of ectoderm to form the neural tube. With the publication of the work of Schwann (1839) and the subsequent emphasis laid on cellular structure, it was held that the histology of the dura mater was essentially that of a connective tissue membrane. Thus, the meninges were grouped embryologically with those structures arising from the mesenchyme.

As a result of the description of Kölliker [2] and His,[3] this view became firmly established and the account of the development of the meninges given by these investigators has remained not only the ortho-

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1. Weed, L. H.: The Development of the Cerebrospinal Spaces in Pig and in Man, Contributions to Embryology, 14, Carnegie Institute of Washington, Publication 225, 1917.

2. Kölliker, H.: Grundriss der Entwickelungsgeschichte des Menschen, Leipzig, Engelmann, 1880.

3. His, W.: Die Häute und Höhlen des Körpes, Arch. f. Anat. u. Physiol. 1903, p. 368.

dox but the only view seriously considered until the present time. Confirmatory evidence was advanced by Salvi [4] who termed the perimedullary layer of mesenchyme the "primitive meninx." This view also received support from Sterzi [5] in a study of the comparative anatomy of the meninges. Briefly, he found that in the acrania there is only a fibrous sheath composed largely of circular fibers, analogous in its position to the meninges of the higher forms. The "primitive meninx" carrying vessels and showing perimeningeal spaces is present in the cyclostomes and in the fishes, and represents both the leptomeninx and the pachymeninx of the higher forms. In the urodele amphibia this splits into two layers, the minor being the leptomeninx and, according to our observations, containing fluid spaces corresponding to arachnoidal spaces. In the anura amphibia, this "secondary meninx" becomes further elaborated and corresponds somewhat more closely to the pia-arachnoid of the mammalia. In birds, the leptomeninx or the "secondary meninx," as Sterzi terms it, shows three layers: an inner membrane intimately related to the cord, a middle layer, which is vascular, and an outer limiting endothelial covering. There is also a distinct subdural space. Finally, in the carnivora, this middle layer of the "secondary meninx" takes on the appearance of the arachnoid as seen in man. The phylogenesis of the meninges, as pointed out by Sterzi,[5] seems to correspond with observations in the chick and in man, and with similar investigations by Salvi [4] in the guinea-pig, in the rabbit and in man, and by Claremont [6] in the mole. According to this view both the leptomeninx and the pachymeninx arise from a common primordium, the mesenchyme, and form, almost simultaneously with the appearance of this structure, a perimedullary layer. The latter divides into two layers, the outer forming the dura and the inner the pia-arachnoid. This is brought about according to His [3] by two zones of condensation, the outer being immediately adjacent to the skeletal structures and the inner to the cord. Between these there is a zone of rarefaction which comes to be the arachnoid in the chick of ten or twelve days, and which later becomes entirely separated from the dura. The dura still later becomes differentiated from the neighboring periosteum. While these investigations were in large part based on the study of the development of the meninges about the cord, Weed has described in great detail the same process about the encephalon. In particular, he has correlated the flow of the cerebrospinal fluid with the appearance of the arachnoidal spaces.

4. Salvi, G.: Histogénèse et structure des meninges, Thèse de Paris, 1898.

5. Sterzi, G.: Recherches sur l'anatomie comparée et sur l'ontogénèse des méninges, Arch. ital. de biol. **37**:257, 1902.

6. Claremont: Sur le developpement des méninges chez la toupe (Talpa europea), Arch. de biol. **32**:1, 1902.

His,[3] Kölliker[2] and Hertwig supposed the mesenchyme to be a homogeneous structure arising from the mesoderm and giving rise in its turn to cartilage, bone, muscle and the connective tissues of the body. With the more recent knowledge of embryology the term mesenchyme has lost, in a sense, its specificity, at least in the broad sense in which it was used by Hertwig (1881). It is certain that in the development of this structure, both ectodermal and entodermal components are concerned in so close a manner that it is difficult to differentiate them histologically at later stages. As Lillie[7] says, "The terms mesothelium and mesenchyme have therefore merely descriptive significance in the early embryonic stages. The mesenchyme has no single embryonic significance either as to origin or fate but it is to be regarded as a mixed tissue." Thus, it is now well established that the neural crest cells mingle with the mesenchymal cells in such a fashion that they cannot be distinguished histologically from the other elements in that structure. From the neural crest are derived certain components of the sensory ganglia, cells that surround the nerve processes (the sheath cells of Schwann), and cells that contribute essentially to the growth of certain cartilaginous structures in the head region (Stone[8]). A study of the relatively mature mesenchyme as made by those early investigators who described the development of the meninges reveals no hint of the correct origin of such mesenchymal components. Indeed, the transformation and migration of the primary cells are so rapid that even in early embryos it may be a matter of chance if such changes are observed. The development of this knowledge has been dependent in large part on experimentation.

DIFFERENTIATION BETWEEN LEPTOMENINX AND PACHYMENINX

As a result of a consideration of certain facts regarding the healing of the meninges that had come to our attention during an experimental investigation, it seemed probable that either the pachymeninx or the leptomeninx, and most probably the latter, has a somewhat different derivation from that customarily assigned to it. At least we felt certain that these two structures were not derived at a late period in embryonic life from the same tissue.

If one compares the reaction to injury of the dura and pia mater, a marked difference is apparent. If a portion of the dura is cut away without injury to the underlying pia-arachnoid, the gap is rapidly filled with organizing tissue without any reaction in the structures beneath.

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7. Lillie, F. R.: The Development of the Chick, New York, Henry Holt & Co., 1908.

8. Stone, L. S.: Experiments on the Development of the Cranial Ganglia and the Lateral Line Sense Organs in Amblystoma Punctatum, J. Exper. Zool. **35**:421, 1922.

Mesothelium is formed over its inner face and healing is completed without adhesions (Sayad and Harvey [9]). If, on the other hand, the flap of dura is turned back, the pia-arachnoid beneath the undamaged center of this flap injured and the flap replaced, there is reaction not only in the structures injured but also in the previously normal dura so that inflammation is common to both structures and uniformly results in adhesions (Lear and Harvey [10]). This indicates that there is a marked difference in stability between the lining cells of the dura and those of the pia-arachnoid. The cells of the former which we know to be mesothelium (Key and Retzius,[11] Weed [1]) melt away in the presence of inflammation, while the lining cells of the arachnoid retain their integrity in the presence of adjacent reaction. If both membranes were of the same type of cell with separation relatively late in embryonic life, they would not be expected to react so differently.

Moreover, the pachymeninx is the lining membrane of a skeletal structure and thus most closely allied to the great lining membranes elsewhere, the pleura, the pericardium, the peritoneum and the joint and bursal spaces. On the other hand the leptomeninx is a covering of, and intimately related to, the central nervous system, being in this sense analogous to the neurilemma or sheath of Schwann in the peripheral nerves. To render the analogy complete it is only necessary to recall that His [3] and Kölliker [2] attributed the origin of the sheath cells to the mesenchyme. This was in the main the orthodox view until Harrison [12] demonstrated the derivation of the sheath of Schwann from neural crest cells. The essential experiment was the removal of the neural crest in certain amphibia, which was followed by a deficiency in the spinal nerves of the sensory neuron and its sheath, and of the sheath of the motor neuron.

All these facts suggested the possibility of the origin of the pia-arachnoid from the neural crest cells, and serial sections of the chick and pig embryo were studied for further evidence. It was apparent that in the spinal sections the neural crest cells swept about the entire cord at a period just preceding the emergence of the motor fibers from the zona marginalis and constituted the marginal membrana limitans. It was felt that this appearance strongly suggested the derivation of this membrane from the neural crest cells—enough, at least, to put the question to the test of experimentation.

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9. Sayad, W. Y., and Harvey, S. C.: The Regeneration of the Meninges, the Dura Mater, Ann. Surg. **77**:129 (Feb.) 1923.

10. Lear, M., and Harvey, S. C.: The Regeneration of the Meninges, the Pia-Arachnoid, Ann. Surg. **80**:536 (Oct.) 1924.

11. Key, E. A. H., and Retzius, G.: Anatomie des Nervensystems und des Bindegewebes, Stockholm, Samson and Wallin, 1875-1876.

12. Harrison, R. G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, J. Comp. Neurol. **37**:123, 1924.

MATERIALS AND METHODS

The experimental study of the origin of the meninges was carried out in the spring of 1924 on embryos of *Amblystoma punctatum*. The operative procedure is well known and need not be detailed here. Embryos varying in age from Stages 28 to 30 (Harrison) were used. This particular series of stages was selected because, as Stone [8] has so clearly shown, the neural crest cells at this time are sweeping ventrally over the surface of the underlying neural tube toward their eventual destination (Fig. 1). It will be noted that at this stage the cerebral hemispheres are practically devoid of enveloping neural crest cells while the midbrain possesses dorsolaterally a well marked mass of them. This condition made possible the selection of two series of operations involving the transplantation of parts of the central nervous system. By transplanting the cerebral hemispheres at this stage to the body region of

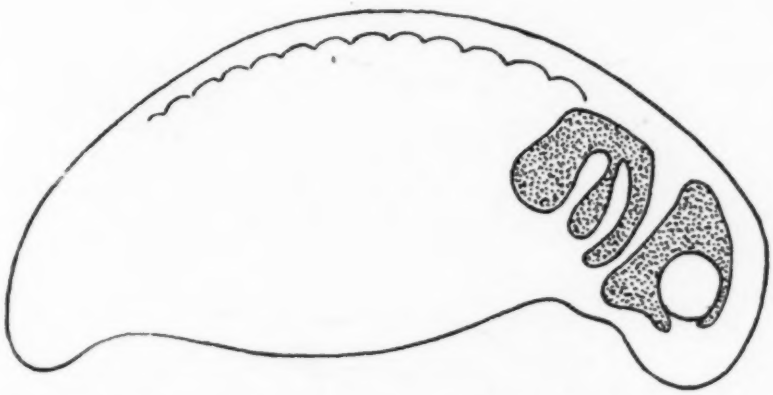

Fig. 1.—Stage 30 (Harrison) after Stone. The stippled area is that of the neural crest cells.

another embryo we should have resulting a fairly typical cerebral hemisphere (Burr [13]) devoid of any transplantable neural crest cells. The objection that neural crest cells from the spinal cord region at the level of the transplantation might envelop the transplant can be ruled out on the basis of the known history of the neural crest cells of this region. It has already been shown that in this region, at this stage, the neural crest cells are in the main distributed to their ultimate destination.

By transplanting a portion of the midbrain at this stage together with the optic vesicle, the epidermis and the mesenchyme and neural crest cells of the region, we have a portion of the neural tube transplanted approximately in its normal environment. Such a transplant

13. Burr, H. S.: The Transplantation of the Cerebral Hemispheres of Amblystoma, J. Zool., **20**, January, 1920.

placed in a new position should have the requisite material, if our premise is correct, for the formation of a fairly typical section of a neural tube, surrounded by the dura and pia-arachnoid. In other words, we have here two series of operations. In Series 1, a portion of the nervous system transplanted without neural crest cells (Fig. 2); in Series 2, a portion of the nervous system transplanted with neural crest cells (Fig. 3).

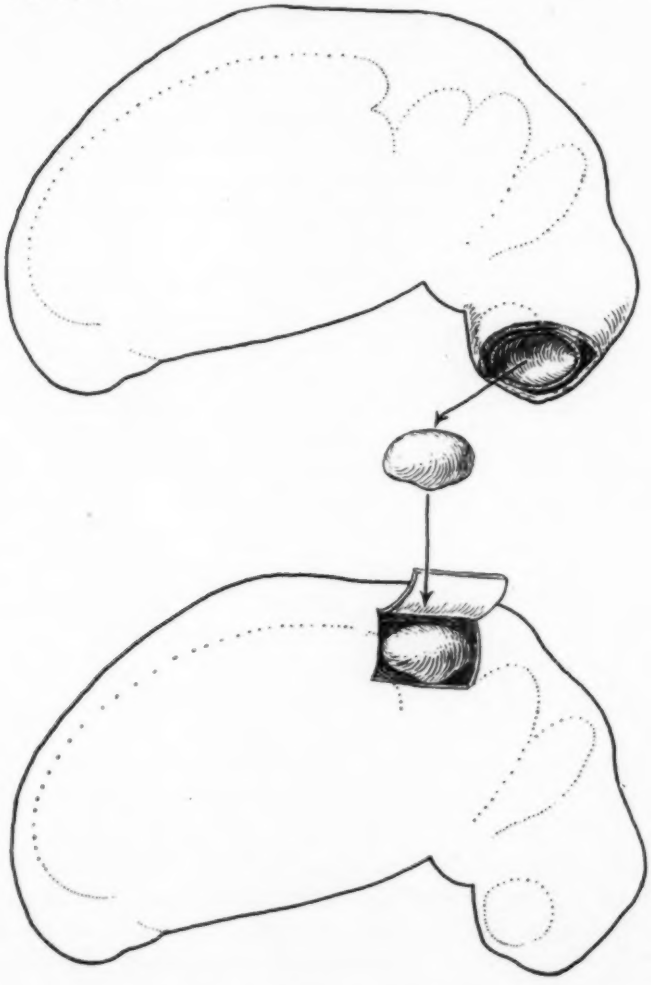

Fig. 2.—Transplantation of portion of cerebrum without neural crest cells.

The experiments outlined above were performed and after the lapse of from one to two months the embryos were fixed in corrosive-acetic acid mixture and stained, some with hematoxylin and eosin and some with Mallory's connective tissue stain.

EXPERIMENTAL RESULTS

The normal meninges in amblystoma do not differ in any essential degree from the brain coverings of the higher forms. Such differences as exist are confined to the degree of elaboration of the structural elements. The dura consists of a thin membrane noticeably thicker than any other similar structure in its surroundings. This thin membrane

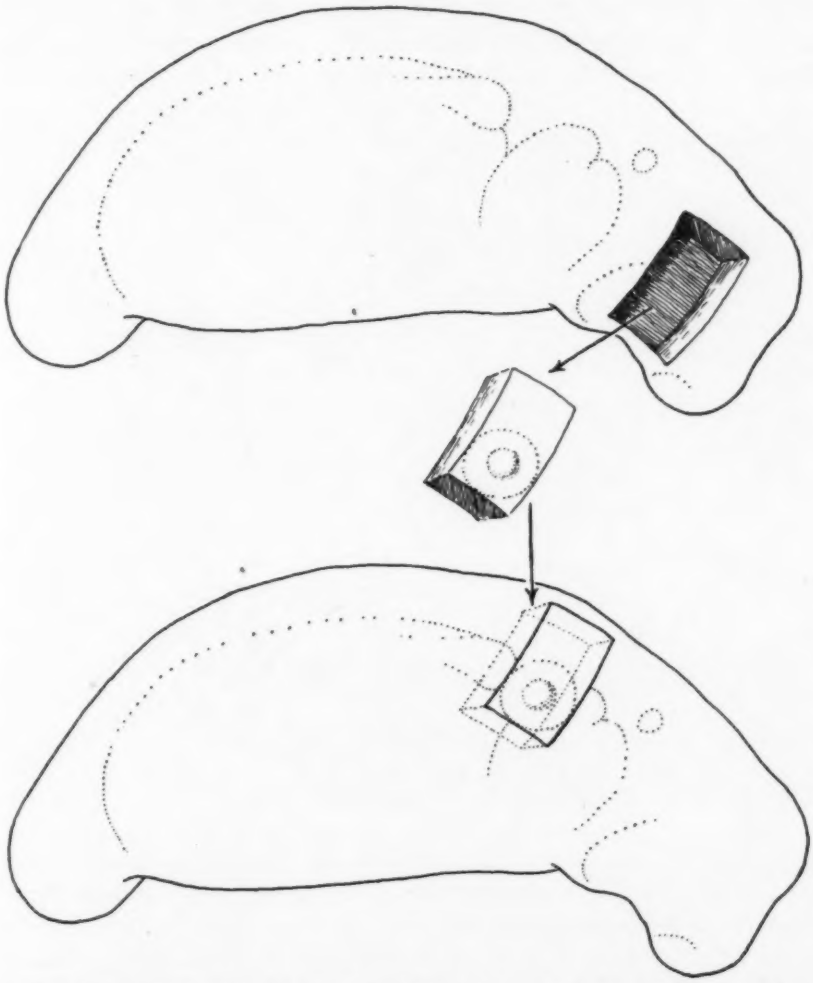

Fig. 3.—Transplantation of cerebral tissue with neural crest cells, mesenchyme and optic vesicle.

bears on its deep surface numerous cells scattered at irregular intervals and conforming to no discernible pattern. The membrane itself lies against the deep surface of the cartilaginous and membranous portions of the brain case (Fig. 4). The pia mater consists of an exceedingly

delicate cellular membrane investing the outer surface of the neural tube. At selected points the pia may be seen to invest the blood vessels which supply the nerve tissue. Stretching from the deep surface of the dura to the outer surface of the pia run numerous fine trabeculae which, in the main, parallel the surface of the neural tube. The cellular elements adjoining these trabeculae are scarce. In fact it is only rarely that one observes a cell nucleus. The trabeculae themselves are united about midway between the dura and pia to form an apparently unbroken sheet completely investing the nervous system. The membrane is in all probability the arachnoid proper. It is connected to the

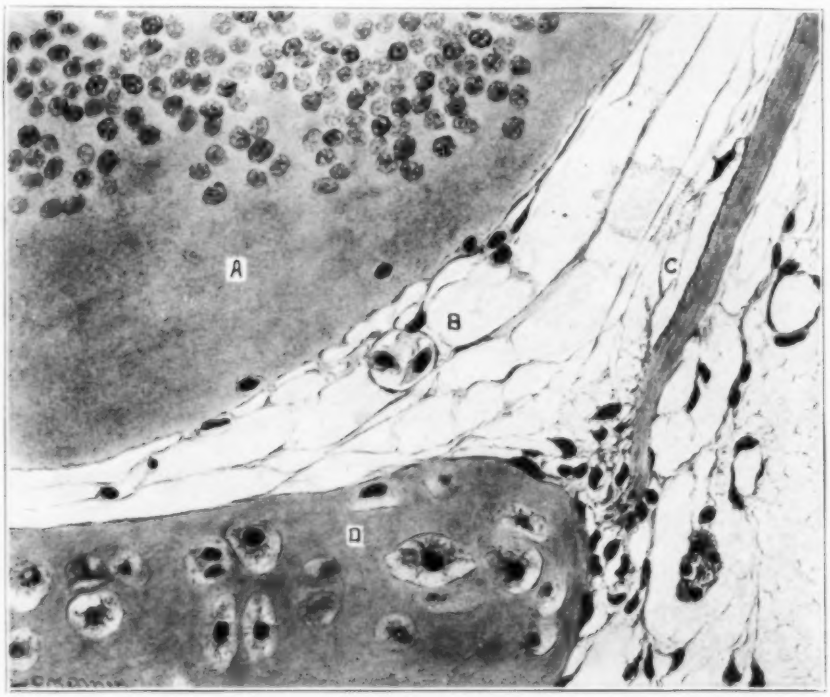

Fig. 4.—A section of the wall of the neural tube and brain case in amblystoma showing a pia-arachnoid investing the brain tissue and including a blood vessel, and a well defined dura forming the lining of the brain case. *A*, neural tube; *B*, pia-arachnoid; *C*, dura; *D*, brain case.

pia by numerous trabeculae, and on its outer surface it establishes contact through fine filaments with many similar filaments, which parallel the deep surface of the dura. Without resorting to experimental methods to determine absolutely the fact, the indications are that the space between the arachnoid and pia is a quite typical subarachnoid space. It is further suggested that the interval between the arachnoid and dura, which is also quite obviously a fluid space, forms a somewhat enlarged

subdural cavity. With these fundamental facts in mind it will be fairly simple to analyze the results of the experiment.

The first series of experiments (Series *Hc*) involved the transplantation of the right cerebral hemisphere to the side of the body between the anterior limb and the gills. The operations were performed on amblystoma embryos (Harrison Stages 28-30). At this stage the neural crest cells in the region of the hemispheres have in the main arrived at their destination, so that if the ectoderm is lifted from the underlying brain tissue there is exposed practically the bare surface of the hemisphere. The few mesenchyme cells which exist can be readily removed by gentle stroking. It will be noticed during this process that the nerve tissue seems to be enveloped by an exceedingly delicate and very incomplete membrane. This likewise can be removed if sufficient care is observed. In preparing the site for the transplanted hemisphere, a semicircular flap of ectoderm was lifted toward the midline and a pocket excavated in the underlying mesenchyme. Into this pocket the bare cerebral hemisphere was placed and the flap of ectoderm returned to its original position. The animals of this series were permitted to live for periods varying from thirty to sixty days, at which time they were fixed in corrosive acetic acid.

The second series of operations (Series *He*) was performed on embryos of Harrison Stages 29-30. The operation consisted in the excision of that portion of the head immediately surrounding the eye. The explant consisted of the eye, the immediate environing ectoderm, the underlying mesenchyme, the neural crest, and the still deeper lying wall of the midbrain. This entire mass was transplanted into the same region as in Series *Hc*, between the anterior limb and the gills. The site of the transplantation was prepared by removing an area of ectoderm and the underlying mesenchyme to a sufficient depth to make room for the transplant. The embryos were allowed to live for periods varying from forty to sixty days. They were then fixed in the same manner as Series *Hc*.

A careful study of the microscopic preparations of the animals in Series *Hc* makes clear the following facts: First, the transplants in the majority of the cases healed into the host in a quite normal manner. The cerebral hemisphere in nearly all instances was quite typical in its organization. This characteristic arrangement of the nerve cells in the transplant indicates again the remarkable potency of the original stimulus for differentiation in the cerebral hemispheres. In this particular series, nerve tissue was transplanted into a completely strange environment separated from its peripheral and central connections, yet, in spite of that lack, a fairly typical hemisphere developed, at least sufficiently typical to be readily recognized. In every instance, however, the size of the transplanted hemisphere was less than normal.

Even a hasty survey of the section showed a distinct difference in the meningeal investments of the transplant from the second series and also from the normal conditions (Fig. 5). This difference manifests itself most strikingly in the complete absence of fluid spaces about the nerve tissue. In other words, when neural tube was transplanted without neural crest cells the transplant developed without its usual fluid covering. Further study showed clearly that the absence of the fluid spaces was due to a complete absence of the leptomeninx (Fig. 6).

Fig. 5.—A low power drawing of a section of amblystoma embryo in which the neural tube was transplanted without neural crest cells. There is no leptomeninx about the transplant. *A*, neural tube transplant; *B*, neural tube of host.

Surrounding the nerve tissue the mesenchyme was condensed to form a fairly definite investment consisting of many fibrous strands, more or less parallel to the surface of the nerve tissue and related to numerous cell nuclei. However, this fairly well organized dural investment in no instance was entirely complete, there being distinct areas in which the mesenchyme showed no definite condensation (Fig. 6). At all points at which the mesenchyme touched the surface of the nerve tissue it seemed to blend more or less distinctly with what appeared to be the

neuroglia supporting framework of the hemisphere. This blending was, in the main, without sudden transition, and only here and there could there be seen any indication of an external limiting membrane of the nerve tissue.

So far as it was possible to determine, blood vessels penetrating the nerve tissue were entirely absent, and only very rarely could a blood vessel be discerned in proximity to the surface of the transplant. This

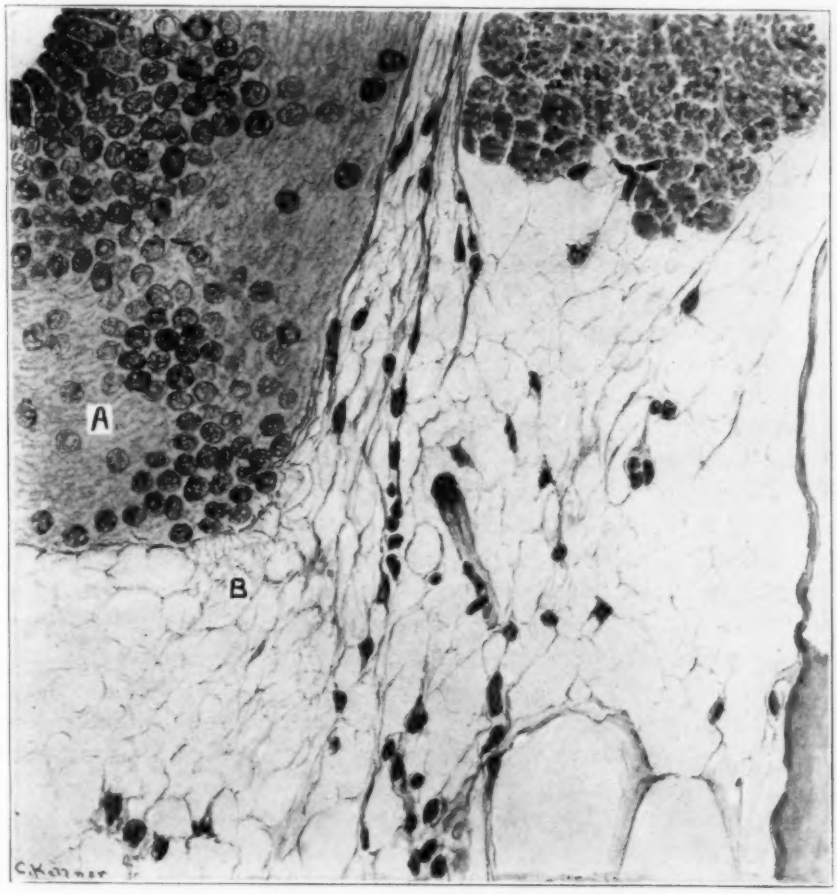

Fig. 6.—A high power drawing of the same embryo as Figure 5, showing the condensed mesenchyme closely related to the neural tube without intervening leptomeninx. *A,* neural tube transplant; *B,* mesenchyme.

is a further indication of the lack of leptomeninx or vascular membrane for the transplant. In one instance, several blood vessels could be discerned close to the portion of the transplant which represented the septum of the hemisphere. There was here no attempt of the ependymal membrane to invaginate to form a choroid plexus.

The results in Series *He* were no less clear. The transplant healed in position with surprisingly few abnormalities. In the majority of instances the eye of the transplant maintained its usual relations to the nervous system. In some instances the eye lay close to the surface with a clearly developed lens and cornea. The latter, however, was usually covered by a layer of typical ectoderm. In spite of the closeness of the eye to the nerve portion of the transplant, no trace of an optic nerve could be found. This is the more remarkable since the relations of the optic cup to the wall of the midbrain are not disturbed by the operation. Furthermore, in at least two instances, after some forty days, the rudimentary lens was the only remnant of the optic cup. The lack of direct nervous connection between the eye and the transplanted portion of the midbrain is peculiar and rather unexpected. Its significance at present is obscure. In two instances the optic vesicle was apparently incorporated in the nervous tube. In one instance the only remnant of the optic cup discernible was the presence of the rudimentary lens and some of the typical retinal pigment.

Even a cursory study of the sections under low power shows beyond question the very obvious difference dependent on the presence or absence of neural crest cells. There is a very marked difference between the meningeal coverings of this series in which the neural crest cells were carried with the transplant and those of Series *Hc*. First, there is a very obvious dura forming a well defined membrane surrounding that portion of the transplant which was removed from the wall of the neural tube (Fig. 7). This dural investment is not closely applied to the nerve tissue except in those locations in which the adjacent structures press closely on the neural tube of the transplant. The clearly defined interval between the dura and the nerve tissue has all the characteristics that may be seen in the normal salamander (Fig. 4). The dura itself forms a lining for such cartilages as have been included in the transplant forming a sharply delimited covering for them. It is possible that the number of nuclei is slightly greater in the dura in the experimental material than in the normal. Immediately surrounding the nerve tissue itself is a distinct delicate nuclear membrane. Blood vessels are included in this delicate covering, which is unquestionably the vascular portion of the leptomeninx, the pia mater.

Stretching from the deep surface of the dura to the outer surface of the pia are many fine trabeculae showing possibly a slightly less concentric arrangement than normally but, nevertheless, nucleated and obviously including fluid spaces (Fig. 8). In nearly every one of the transplanted embryos of this series there was present a more or less complete choroid plexus, developed in every instance in the ependymal curtain, which forms across the cut surface of the neural tube. Blood

vessels were always present adjacent to the ependymal curtain. This would seem to indicate a causal relationship between blood vessels and the formation of a choroid plexus in the ependymal wall of the neural tube (Fig. 7). In only one instance in Series *Hc* did anything develop which looked like a choroid plexus, and detailed examination showed that this was due to the fact that the tubules from the pronephros had invaginated the ependymal wall of the nervous transplant.

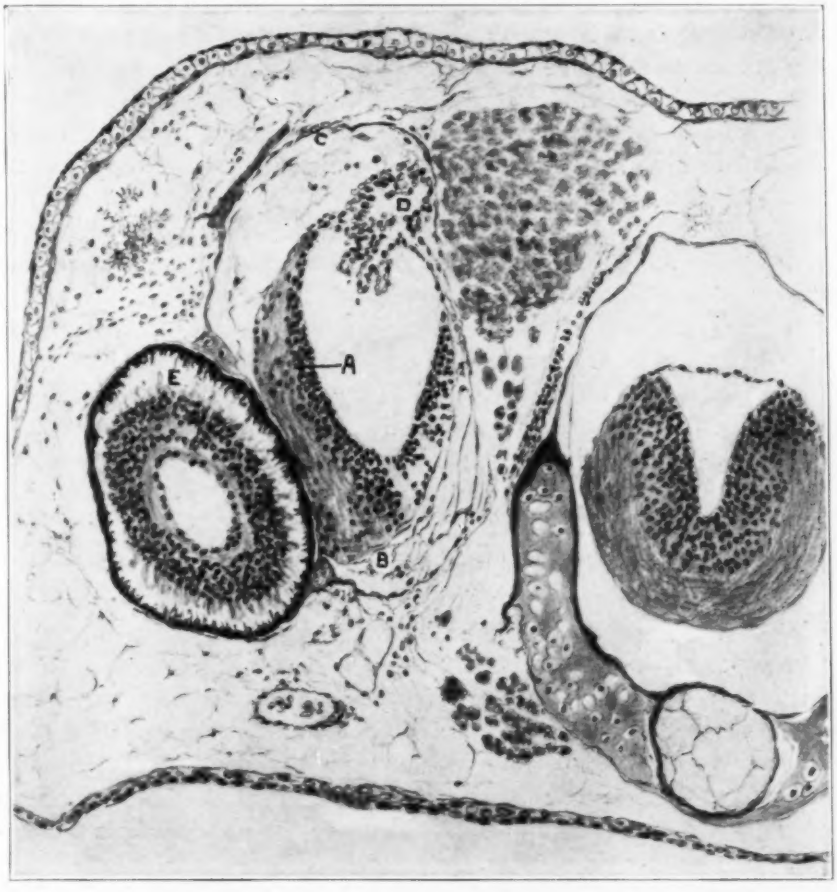

Fig. 7.—A low power drawing of a transplanted neural tube with neural crest cells showing the dura, pia-arachnoid and a choroid plexus. *A*, neural tube transplant; *B*, pia-arachnoid; *C*, dura; *D*, choroid plexus; *E*, optic vesicle.

It seems to be reasonably certain, therefore, that the neural crest cells in the head region are the source from which develops the leptomeninx in amblystoma embryos. The fact that in those embryos in which the transplant lacked neural crest cells it was devoid of pia and arachnoid, while in those with transplants possessing neural crest cells there was a

clearly defined leptomeninx, makes the foregoing statement reasonably certain. That the dura is not involved in the fate of the neural crest cells is evidenced by the fact that a more or less well developed pachymeninx was found in both series.

COMMENT

The inferential deduction that the leptomeninx and the pachymeninx have a separate embryologic derivation is confirmed by the experiments on *Amblystoma*. Moreover, it is definitely proved that the leptomeninx arises from the neural crest cells early in embryonic life and that the pachymeninx takes origin in the mesenchyme at a relatively later period. With this knowledge at hand one can follow in a more detailed fashion the development of these structures. This discussion is largely based on observations in the chick embryo, but in part on the pig embryo, particularly in the later stages. For the purpose of correlation and amplification of these observations, free use has been made of "The Development of the Chick," Lillie,[7] and of "The Development of the Cerebrospinal Spaces in Pig and in Man," Weed,[1] and also the articles of Landacre,[14] Harrison [12] and Stone.[8]

In considering the embryologic history of the neural crest cells, of which the formation of the leptomeninx is but one episode, it is more convenient to divide it into stages, such as the formation of the neural crest; the migration of the neural crest cells; the differentiation into leptomeninx.

THE FORMATION OF THE NEURAL CREST

The neural crest in the chick, which is a cord of ectodermal cells lying in the angle between the neural tube and the ectoderm proper, first appears anteriorly at the sixth and seventh somite stage. From this it extends progressively posteriorly, simultaneously with the closure of the neural tube. The preotic portion is well developed at the stage of from seven to eight somites and rapidly undergoes a process of migration. The postotic division may be observed in different degrees of formation, as one examines caudad, up to the stage of from twenty-seven to twenty-eight somites.

The preotic development of the neural crest takes place in the chick in a somewhat different manner from that of the postotic and may be conveniently considered in two divisions, that overlying the forebrain and midbrain, and that in the region of the trigeminus and the acousticofacialis. In the former the neural crest is seen very early, is very transitory and passes rapidly into the formation of the mesenchyme, the

14. Landacre, F. L.: The Fate of the Neural Crest in the Head of the Urodeles, J. Comp. Neurol. **33**:1, 1921.

greater part of which, lying cephalad to the optic vesicles, seems to be of ectodermic derivation. In the latter, the neural crest spreads out into plates which soon become involved in the formation of the great sensory ganglia of this region and immediately meet the mesenchyme arising in the vicinity of the foregut, intermingle with it, and to a great extent lose their identity. In the postotic development, the crest first appears as a cap which shows metameric beading and develops in relation to the somite. This formation is best seen in the embryo during its growth up to the stage of ten somites or in the first thirty hours of incubation.

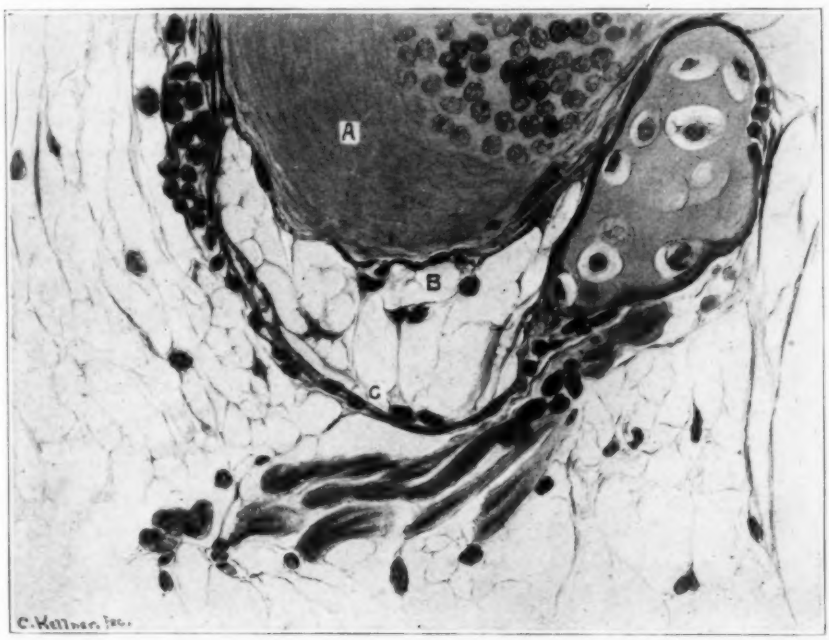

Fig. 8.—A high power drawing of a transplant of the same series as Figure 7, showing the dura and pia-arachnoid about the transplanted neural tube. *A*, neural tube transplant; *B*, pia-arachnoid; *C*, dura.

THE MIGRATION OF THE NEURAL CREST CELLS

The migration of the cells at the cephalic pole of the embryo occurs almost simultaneously with their formation (Fig. 9). Indeed, in the chick it is a question whether the ectoderm over a considerable area does not function as does the neural crest in forming mesenchyme. At least, the greater portion of the mesenchyme in the early stages lying cephalad to the tuberculum posterius is of ectodermic origin. It soon loses its identity, however, and presumably becomes intermingled with mesenchyme derived from the entoderm extending forward from the

region of the oral plate and the foregut. Such mixed mesenchyme surrounds the entire telencephalon, and from this are differentiated, at a later date, the pachymeninx and the leptomeninx.

In the region of the diencephalon and the mesencephalon or from the tuberculum posterius to the otic vesicles the progress of migration is

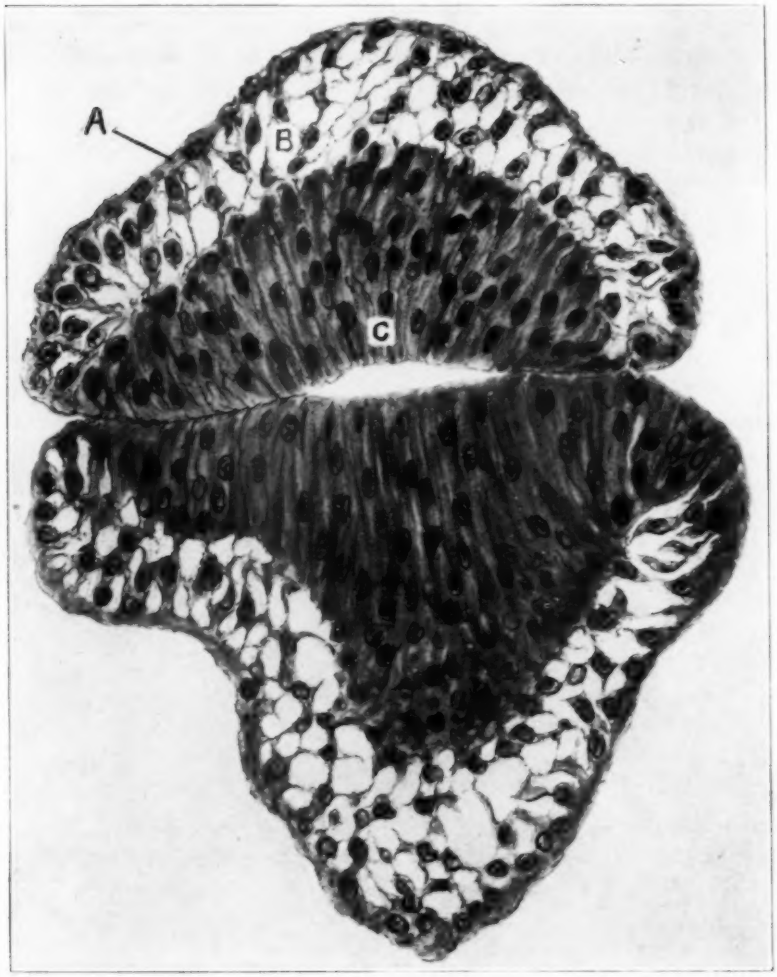

Fig. 9.—Section through the anterior portion of the telencephalon in a chick embryo of seven somites. The mesenchyme is in large part being directly derived from the ectoderm. *A*, ectoderm; *B*, mesenchyme; *C*, telencephalon.

less simple, as the neural crest cells here have to do with the formation of the sensory ganglia, the sheath cells of the peripheral nerves (Harrison [12]) and certain of the cartilages of the branchial arches (Stone [8]). At first, the migration takes place as a solid sheet, extending outward

from the neural crest on either side and giving rise to the major portion of the dorsal mesenchyme in this area (Fig. 10). In the amblystoma (Stone [8]) and other urodeles (Landacre [14]) this migration continues ventrad and the neural crest cells enter into the formation of cartilage in the branchial region. Presumably the same is true in the higher vertebrates, although this has not yet been proved. Migration also takes place directly about the neural tube so that there are neural crest cells present ventrally, as well as dorsally and laterally, and these presumably form the anlage for the leptomeninx in this region.

The process at this level is more complicated because of the development of the branchial arches and of the sensory ganglia, but posteriorly in the somatic areas it is somewhat simpler. The cap of crest cells which appears with the closure of the neural tube extends outward on either side forming first a triangle, and then a sheet of cells which lies in the angle between the neural tube and the ectoderm. More cells soon establish contact with the myotomes and then pass ventral between these structures and the neural tube. The next step is the aggregation of certain of these cells into a compact group in each somite which later becomes the ganglion of a sensory nerve. Concomitant with the formation of the mantle zone there is migration to the ventral surface of the cord so that the entire tube is invested and the motor nerves as they emerge from the cord receive their sheath components (Fig. 11).

THE DIFFERENTIATION INTO LEPTOMENINX

Following the migration of the neural crest cells into the mesenchyme and about the neural tube, there remains a cellular layer, two or three cells in thickness, which is closely related anteriorly with the mesenchyme and posteriorly with the ganglia and nerve roots. In this and immediately in contact with it are developed the blood vessels of the pia. At a later stage this thins out to form the inner layer of the leptomeninx. In certain areas, as in the roof of the fourth ventricle, it disappears altogether and allows for the passage of cerebrospinal fluid from the ventricles into the arachnoid. The differentiation of the arachnoidal components of the leptomeninx is, according to Weed,[1] dependent on the presence and circulation of cerebrospinal fluid and first appears in the basilar portion of the encephalon. Certainly, the appearance is that of the distention of intercellular spaces in the mesenchyme by fluid. The bulk of the process takes place at about 18 mm. in the pig embryo. In places, as over the cerebral hemispheres, the trabeculae persist, whereas, about the cord and in the basilar cisternae the mesenchyme is spread into two layers. In either case the fluid spaces are lined by low cuboidal epithelium derived from either the neural crest cells in the mesenchyme or those lining the neural tube. The last stage in the formation of the arachnoid is the differentiation of the outer layer of

the arachnoid. This occurs at the time of the condensation of the mesenchyme which forms the dura and subsequent to the dilatation of the arachnoidal spaces with fluid. The process gives an impression as of a pressing outward of mesenchymal tissue, thus causing a layer of cellular condensation. It is possible that that portion of the mesenchyme rich in cells derived from the ectoderm is penetrable to the fluid and distends into spaces, while that portion which is mesenchyme of the

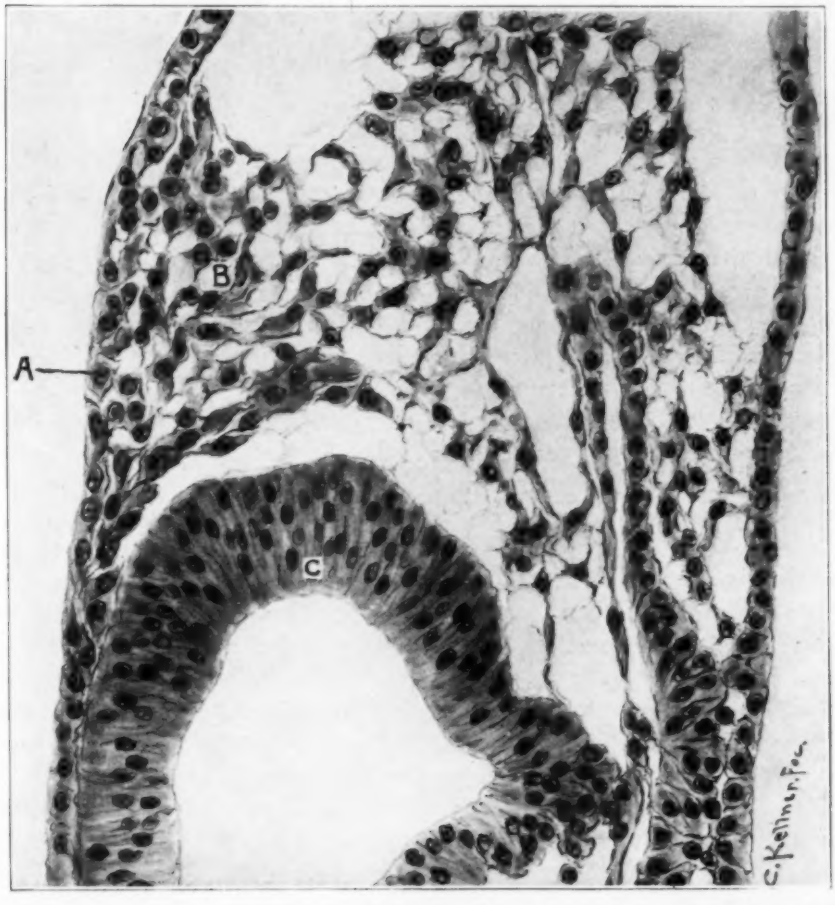

Fig. 10.—Section immediately posterior to the optic vesicle in a chick embryo of eight somites. The dorsal half of the mesenchyme is being derived from the neural crest. *A*, ectoderm; *B*, neural crest cells; *C*, neural tube.

usual variety is impenetrable and is pressed outward by the distending spaces within. In this fashion a layer of ectodermal cells may come to lie on the outer surface of the arachnoid and a similar layer of mesodermal cells on the inner surface of the dura; in any case this is the final result of the differentiation of the leptomeninx and the pachymeninx.

THE SIGNIFICANCE IN DISEASE OF THE DERIVATION OF THE LEPTOMENINX FROM THE NEURAL CREST

As has been pointed out in a previous paper (Lear and Harvey [10]), the leptomeninx possesses, as might be expected from the specificity of its derivation, certain characteristics of reaction. It reacts so slightly to an aseptic injury of the overlying dura that it suffers no permanent loss of continuity; in other words, it does not become adherent. If the continuity of its surfaces is broken, the mesothelial lining of the adjacent dura rapidly enters into the reaction of repair and an adhesion occurs.

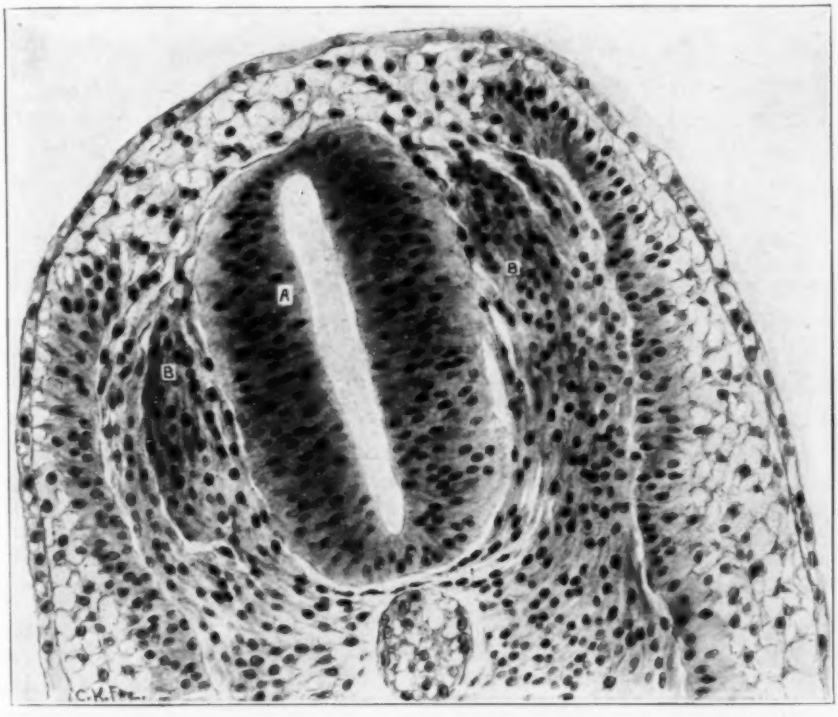

Fig. 11.—Section through a somite in the chick embryo of from thirty-two to thirty-four somites. Cells of neural crest derivation, continuous with those of the sensory ganglia, extend about the neural tube. *A*, neural tube; *B*, sensory ganglia and cells of neural crest derivation.

It is apparent then that adhesions between the pachymeninx and the leptomeninx need suppose only a sufficient injury to the latter to impair definitely the vitality of its outer surface.

As to how great such an injury need be, there is little information at hand. Trauma as slight as the scratch of a needle, the rubbing by the pulsation of the brain of a silk suture or the rough edge of a spicule of bone, is sufficient as we know from experimental data. A blood clot is

not sufficiently injurious, but it is quite possible that the presence of an heterotonic solution may be. As has been shown by Esseck,[15] the presence of laked blood induces the lining cell of the arachnoidal spaces to become phagocytic, to dissociate itself from its neighbors and to wander forth, closely resembling in appearance the macrophage of Metchnikoff. Whether such reaction is sufficient to impair the continuity of the lining is a subject for further experimentation. Presumably, actual death of the lining cells is necessary.

Certainly the work of Esseck[15] indicates that a relatively minor injury is sufficient to induce a cellular reaction in the interstices of the arachnoid, and this is corroborated by the clinical evidence of reaction following the introduction of serums or other medication with the consequent "serous arachnoiditis." If such a reaction is intensified, as it is in an infectious leptomeningitis (Ayer[16]), then actual destruction of lining cells may take place both within the interstices and on the surface of the arachnoid, sufficient to lead to cicatrization and the formation of adhesions.

That adhesions, as has been commonly assumed, may be caused only by such a severe injury does not necessarily follow. Dandy[17] has shown that a considerable number of children born with "communicating hydrocephalus" have a block in the flow of cerebrospinal fluid due to adhesions around the foramina in the roof of the fourth ventricle, in the basilar cisternae or in the pathways of flow over the cortex. It is quite possible that this condition represents a defective development of the arachnoidal spaces, an hypothesis that is not untenable when one considers the method of their formation.

The origin of the leptomeninx in the neural crest ectoderm is probably of greater significance, however, in respect to the neoplasms of this membrane. Cushing and Weed[18] have strongly suggested the derivation of the endotheliomas and psammomas of the meninges from "arachnoidal inclusions." Why inclusion of one mesothelial tissue in another, both of late and identical origin, should lead to such character-

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15. Esseck, C. R.: The Formation of Macrophages by the Cells Lining the Arachnoid Cavity in Response to the Stimulus of Particulate Matter, Contributions to Embryology, 42, Carnegie Institute of Washington, Publication 272, 1920, p. 377.

16. Ayer, J. B.: A Pathological Study of Experimental Meningitis from Subarachnoid Inoculation, Monograph of the Rockefeller Institute, 12, 1920, p. 26.

17. Dandy, W. E.: The Cause of So-called Idiopathic Hydrocephalus, Bull. Johns Hopkins Hosp. **32**:67 (March) 1921.

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istic neoplasms has been a little difficult to understand. Knowing that such inclusions are of cells derived originally from the ectoderm makes this hypothesis more than probable. Many others of the bizarre tumors associated with the meninges, the ganglia, the peripheral nerves and the sympathetic system may, on further study with this point in mind, fall into a common group of neoplasms having their derivation in the neural crest cells. The nomenclature of such tumors has always been most unsatisfactory and many times misleading. This is the result of confusion as to the type of cell from which they originate. Such as are considered to have arisen from cells of neural crest derivation might well be called neurolophoblastomas (λόφος, crest) or in a less cumbersome manner, neurolophomas.

SUMMARY

The view of His and Kölliker, supported by Salvi, Sterzi, Weed and others, that the pachymeninx and the leptomeninx have a common origin in a primitive mesenchyme derived from a specific germ layer, the mesoderm, is incorrect.

Certain ectodermal elements derived in large part from the neural crest are contributed to the mesenchyme and take part in the formation of the leptomeninx.

These facts have been demonstrated experimentally in *Amblystoma* and are confirmed by observations in the chick and pig embryo.

Such origin suggests that the cells of the leptomeninx may have certain characteristics of their own, apparent in their reaction to injury and in the neoplasms arising from them.

DISCUSSION

Dr. Frederick Tilney, New York: I think it only fair to say that in the light of modern orthodox embryology, this contribution is a thorough-going piece of heresy. On the other hand, heresy has a certain peculiar value of its own. I believe that the contribution which Dr. Harvey has given us is particularly significant in its tendency to depart from the diagrammatic notions of embryology to which we are more or less wedded. The idea that these three layers of the embryo have a specificity in their derivatives is losing ground, I think, year by year. To show that the derivatives from the outer layer, the ectoderm, have a capacity for developing definitely connective tissue elements with the formation of blood vessels is something that should be welcomed as a particularly inspiring thought from our present point of view on the derivation of tissues connected with the nervous system.

I feel very grateful to Dr. Harvey for a particular reason; that is, he has given me a clew to understand how the central nervous system may develop isolated blood islands of its own and become vascularized without a necessary invasion from the outlying mesoderm or mesenchyme of the leptomeninges.

Dr. Casamajor and I made some investigations a few years ago from which we showed in the rat that vascularization took place independent of the extrinsic

vessels. We thought it was due to an invasion from the outlying mesenchyme, but our evidence was scant in this particular and we were very doubtful as to whether we had proved our point.

If, however, it is possible for the ectoderm to give rise to a vascularization such as this, I think it is a very acceptable view and far from heresy. It seems to be in the right line of interpretation.

Dr. Harvey Cushing, Boston: We have listened this afternoon to a paper based on comparative anatomy, to one which concerns experimental pharmacology, and now to one in which experimental embryology has been brought into play, and I add my word of congratulation to Dr. Harvey on what I think a most brilliant study. None of us can fail to be other than struck by the various ways that lie open to us, as people interested in neurology, to attack our many problems.

One question comes to my mind, which I hope Dr. Harvey may answer. I understood that in the case of the primary transplant the choroid plexus was not included, whereas in the secondary transplant, which included the neural crest, the plexus was included. If I understand Weed's views correctly, he lays stress on the secretion from the plexus in the development of the fluid spaces of the arachnoid and finds that these spaces begin to form when fluid finally seeps through the tela choroidea into the enveloping mesenchyme. On this basis, if merely the anlage of the brain itself were to be transplanted, one would hardly expect to find either fluid or arachnoid spaces.

Dr. Harvey also spoke of the relation of this subject to tumors of the nervous system; and if we accept his novel view that the nerve sheathes themselves and the leptomeninges have a common development, I think that it explains better than any other way the widespread lesions of von Recklinghausen's disease. For in this disease we have a disorder characterized by multiple tumors, the exact origin of which we have never been quite clear about. The fact that many of these patients with generalized neurofibromatosis have at the same time multiple tumors of the meninges, which I personally believe are tumors that develop from the arachnoid rather than from the dura, leads one to assume that in this condition we have represented a neoplastic disorder which is due to a congenital derangement of the entire system which Dr. Harvey has described.

Dr. Byron Stookey, New York: Some years ago Ross Harrison cut off the ganglionic crest of a frog and showed that the peripheral nervous system was derived in the main from the ganglionic cells and also the neural cells forming the sheath of Schwann, but he failed to show that it was derived from the ganglionic crest.

I would like to ask Dr. Harvey if he does not think that his researches perhaps point to a different origin for the endoneurium and perhaps a different origin for the peripheral nervous system? It seems to me that his very brilliant researches would point toward a differentiation of these three membranes, perhaps, making the endoneurium and perineurium and epineurium, and therefore finding a point of contact for the origin of the tumors of the peripheral nervous system which seem so much like the tumors of the central nervous system.

Dr. Samuel C. Harvey: In regard to Dr. Stookey's suggestions, it is quite true, and I would like to emphasize the fact, that the idea of this work is essentially the same idea as Harrison's; and if Harrison had not carried through his line of experimentation so thoroughly, and to every one's satisfaction proved his

point experimentally, this would have been quite impossible. The two are very closely correlated. Dr. Cushing's suggestion that it may mean a correlation of the peripheral nerve tumors with those tumors arising from the leptomeninx is also a probable one.

As to Dr. Cushing's question in regard to the choroid plexus, the choroid plexus at the time of the transplantation is not yet developed, so that there is no transplantation of the choroid plexus; there is a transplantation of the neural crest cells. It is possible that the choroid plexus is not entirely responsible for the extension of fluid spaces into the arachnoid.

VASCULAR LESIONS AND TUMORS OF THE BRAIN DIFFICULTIES IN DIFFERENTIAL DIAGNOSIS

REPORT OF SEVEN CASES WITH NECROPSY FINDINGS *

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The diagnostic ability of the neurologist is often put to an extreme test when he is asked to decide whether a middle-aged patient with moderate hypertension has a neoplasm or some form of vascular lesion of the brain. Instances of cerebral neoplasm are not uncommon in which the onset of symptoms is very sudden, almost precipitate, and the subsequent clinical course may be so rapidly progressive and so strikingly lacking in the so-called cardinal symptoms of brain neoplasm as to compel the diagnosis of a vascular insult. On the other hand, vascular disease of the brain may frequently unfold a clinical picture, which by its insidious onset and slow development may so simulate a brain neoplasm as to make a differential diagnosis almost, if not altogether, impossible.

A group of such cases has been assembled by us during the past two and a half years, and is here presented.

REPORT OF CASES

CASE 1.—*History.*—R. R., aged 25, who was admitted July 7, 1924, and died July 16, 1924, had been under observation in the hospital on three different occasions. On her first admission, April 14, 1920, she gave a history of having had, three years previously, an attack of acute nephritis. While it was said that she made a good recovery, nevertheless, she soon thereafter began to complain of frequent dull headaches, and there developed evidence of hypertension. The symptoms grew progressively worse, and shortly before admission to the hospital her condition became markedly aggravated by greater intensity of headache, frequent attacks of vertigo, dyspnea and dull pain in the precordial region.

First Admission.—Physical examination at this time revealed definite enlargement of the heart, the left border being 9 cm. from the midsternal line in the fifth interspace. The heart sounds were loud and booming with a short systolic murmur at the apex, and there was a ringing second aortic sound. The urine, aside from a trace of albumin, gave negative findings. The phenolsulphonephthalein output was 45 per cent. in two hours. The blood Wassermann test was negative. The blood chemistry findings were within normal limits. The blood pressure was 195 systolic and 125 diastolic. The ocular

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fundi showed definite arteriosclerotic changes. There was no elevation of temperature. The patient was thought to have chronic interstitial nephritis with hypertension. She remained in the hospital for a short time, and went home against advice in an unimproved condition. She remained at home for about four years, complaining almost constantly of headache, until six weeks before her second admission to the hospital, June 5, 1924, when a sudden change in her condition took place. Her headache became very severe and almost constant, and she began to vomit frequently. Her vision became impaired and continued to fail. With this, weakness in the extremities developed.

Second Admission.—On her second admission to the hospital the following findings were recorded: the head was held with a left cerebellar tilt, and there was slight tremor of the head, slight ptosis of the left upper eyelid, bulging of the left eye, slight lateral nystagmus to the right and bilateral corneal hypesthesia. There was irregularity of the pupils, the left being larger than the right; the left pupil reacted poorly to light, the right was not very prompt; both pupils reacted well in accommodation. The jaw was drawn to the left and downward, and there was a left facial weakness. There was left adiadokokinesis and cerebellar form of hands which was more marked on the left side. There was ataxia in the left arm, faulty recoil in both upper extremities and weakness in both arms. The reflexes in upper and lower extremities were greater on the right than on the left. Hearing was impaired on the left side. There was bilateral papilledema.

The symptoms and signs were regarded as pointing to a neoplastic process in the left cerebellar hemisphere, and suboccipital decompression and exploration of the posterior fossa was performed. No neoplasm was found, but marked arteriosclerotic changes in the vessels on the surface of the cerebellum and a peculiar yellowish discoloration of the left cerebellar lobe were noted. There was no change in consistency, and no fluctuation in that lobe was felt.

Following the decompression there was rapid improvement as shown by the subsidence of the objective neurologic findings, disappearance of the headache, marked reduction in the swelling of the optic disks, return of power in the extremities and, finally, return of normal station and gait. The patient remained fairly comfortable for a period of two weeks; then her condition began to decline, and she suffered from headache, dizziness, vomiting and emotional instability with periods of irrationality.

Third Admission.—The patient was readmitted to the hospital, July 7, 1924, with: conduct disorder and restlessness demanding restraint; speech disturbance of the character of motor aphasia; staggering gait; tendency to fall to the left; bilateral external rectus weakness; left corneal hypesthesia; left facial weakness; deviation of the tongue to the right; hyperreflexia on the right side; diminution of abdominal reflexes on the right; bilateral Babinski sign, more marked on the right; adiadokokinesis on the left side, and bilateral papilledema going on to atrophy. The blood pressure was 250 systolic, and 170 diastolic. In view of the aphasia and previous negative findings on suboccipital exploration, the possibility of a left frontal neoplasm was considered and ventriculography was suggested for the purpose of localization. This was carried out, but soon after the injection of air, the patient began to fail, and she died a few hours after the operation. The necropsy was limited to the cranium.

Gross Anatomy.—The dura was adherent to the skull and underlying pia-arachnoid in the region of the original suboccipital decompression, but was otherwise normal. The pia-arachnoid was smooth and glistening, and was

adherent to the posterior lobes of the cerebellum. The pial vessels presented numerous atheromatous areas in the form of narrow, yellowish rings, somewhat raised on the surface of the vessels. The brain showed marked flattening of the gyri. On the removing of the brain, the cerebellum appeared firmly attached to the overlying meninges, making it necessary to break the adhesions forcibly; in this way, parts of the posterior lobe of the cerebellum which were attached

Fig. 1.—Sections of brain stem and cerebellum in Case 1, showing the hemorrhagic cyst and adjacent small areas of softening.

to the meninges were torn, opening a large cavity filled with blood and extending deep into both cerebellar hemispheres. The left cerebellar hemisphere, however, seemed to be more involved than the right. The vessels at the base of the brain, their tributaries and branches showed marked atheromatous changes. The vertebral arteries, however, were most markedly thickened, the right being almost occluded. Not a single vessel was found free from these

changes. The appearance of the vessels in the areas in which the lesions were more pronounced was striking, showing small, yellowish white elevations that gave the appearance of nodules.

On sectioning of the brain the following changes were found in the cerebellum: a section through the middle cerebellar peduncles presented a large cystic cavity (Fig. 1), elliptic in outline, with the long axis in the dorsoventral direction. It was about 4 cm. long by 2.5 cm. wide. Its lining was rough, granular and dark brown in appearance, and not well demarcated from the adjacent brain tissue. Hard, coagulated blood was found adherent to certain areas of the wall of the cyst. There was evident softening in the neighborhood of the cyst with small excavations here and there about its wall for a distance of about 1 cm. Small hemorrhagic foci were also seen in the vicinity of the cyst. These hemorrhagic foci and the areas of softening gave a moth-eaten appearance to structures adjoining the cyst. There was direct communication between the cyst and the fourth ventricle. The latter was almost completely filled with a dark brown hard thrombus of fairly recent origin. The aqueduct of Sylvius was also completely occluded by a similar mass of hardened blood, while the third and lateral ventricles, which were definitely hypertrophied (Fig. 2), were filled with still liquid blood containing small, recent thrombi.

Other areas of softening of various sizes were found, most extensively in the left putamen. The lenticular nuclei were extremely soft in consistence, in marked contrast to adjacent portions of the brain.

Microscopic Anatomy.—Sections through the cerebellum presented the histologic features of an extensive softening process surrounded by areas in which there were glial reactions, adventitial infiltrations and proliferations. Vessels with marked arteriosclerotic changes were seen in the cerebellum and other portions of the brain, including the cerebral cortex and brain stem.

Comment.—This case may be regarded as belonging to the uncommon group in which arterial disease occurs in early life. The history gave definite indication of both arterial and renal involvement, and the exploratory craniotomy also revealed the presence of arteriosclerotic vessels on the surface of the brain, which, in conjunction with the history, should have given warning that the condition was vascular rather than neoplastic. A tumor might have coexisted with the arteriosclerosis and could then have been excluded only by demonstration of an internal hydrocephalus by means of ventriculography. We shall show in a subsequent case that this method is not absolutely reliable with tumors in the posterior fossa.

Case 2.—U. S., aged 45, a tailor, who was admitted April 18, 1923, and died May 13, had been taken ill four years before when he had suddenly developed paralysis of the right side of the face. Power returned at the end of four days, but following this attack a change in personality was noticed. He was thought to be irrational at times and was restless and easily excited. His vision began to fail and he had to give up work. He had occasional incontinence of urine, and it was noted that he dragged his right leg and that a tremor developed in his right arm. Later he became emotionally unstable; he would cry and laugh on slight provocation. His memory and orientation became impaired, and his general condition was rapidly declining.

Physical Examination.—The patient was apathetic, and it was difficult to hold his attention. The pupils were equal, and reacted well to light and in accommodation. The left ocular fundus showed marked engorgement of the

veins which were not tortuous. There was slight right facial weakness, slight weakness of the right leg, ataxia and adiadokokinesis of the left arm. All deep reflexes on the right side were more active than those on the left. A Babinski sign was present on the right side. The right abdominal reflexes were diminished. The blood pressure was 170 systolic, 105 diastolic. The blood Wassermann reaction was negative. The spinal fluid was clear and under

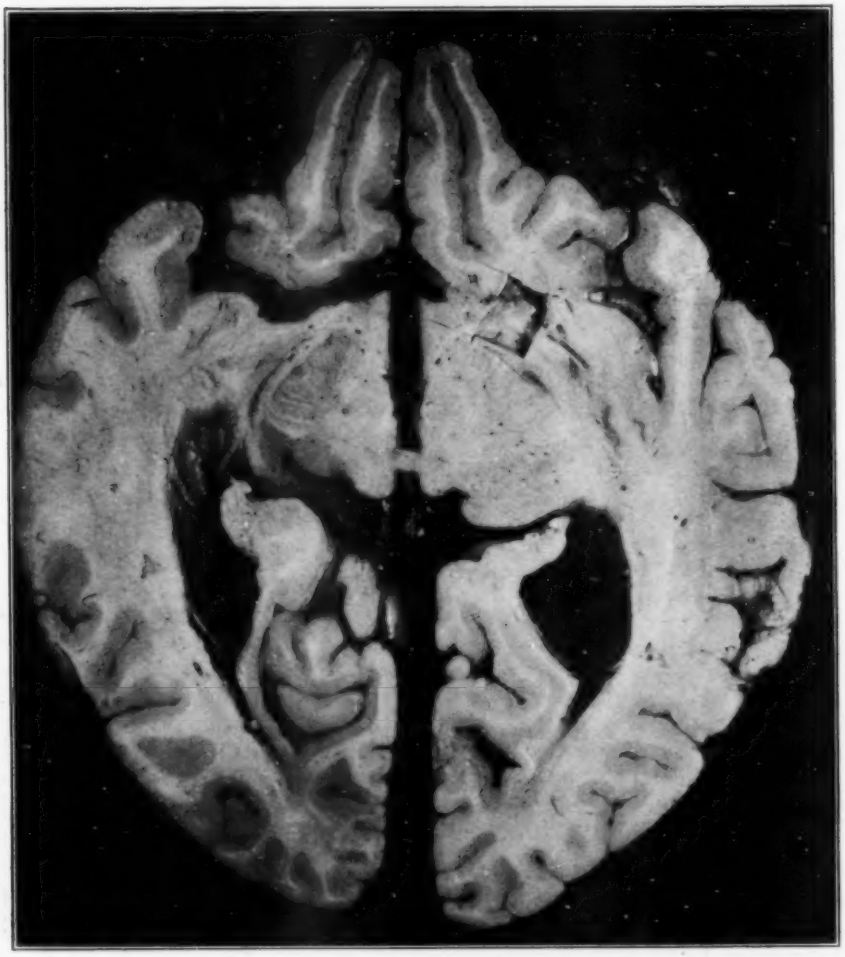

Fig. 2.—A horizonal section of the brain in Case 1, showing marked distention of the third ventricle and of the posterior horns of the lateral ventricle.

normal pressure; it contained 40 cells, and gave a negative Wassermann reaction.

Treatment and Course.—The diagnosis was uncertain; it was difficult to decide between a vascular lesion and a neoplasm in a person with decided hypertension. Ventriculography was performed, and showed no displacement or change in the form of the ventricles. The significance of these findings was not appreciated at that time; the possibility of a neoplasm was still considered,

and an exploratory craniotomy was recommended. This was done in the left frontal region. An aspirating needle passed into the left frontal lobe brought a moderate amount of blood, suggesting a deep lesion situated somewhat posterior to the motor area. No tumor was found. After the operation, the condition of the patient declined rapidly, and death occurred May 13. The necropsy was limited to the cranium.

Gross Anatomy.—When the surgical wound was opened a large organizing hemorrhage was found over the dura. The dura was reflected and a small amount of blood was found covering the surface of the brain. The brain showed a small area of laceration about the middle of the fissure of Rolando. The left cerebral hemisphere appeared somewhat collapsed and flattened, but showed no evidence of increased intracranial pressure. On the incision of the left hemisphere, a cavity measuring about 5 by 3.5 cm. was found involving both the precentral and postcentral convolutions (Fig. 3). The cavity was collapsed, contained a small quantity of blood and presented a rough, irregular inner lining. Further search disclosed an area of softening, yellowish in color and apparently of old standing, occupying the posterior end of the left lenticular nucleus. The vessels at the base of the brain, including the entire circle of Willis, showed very advanced arteriosclerotic changes.

Microscopic Anatomy.—Section through the wall of the cyst showed the lining of the cavity to be covered by fresh blood, underneath which there was a wide zone of softening of brain tissue. In the area of softening, numerous polymorphonuclear leukocytes, mononuclear elements and proliferated glia cells were found. The vessel walls in that area were degenerated and surrounded by leukocytic elements and gitter cells filled with yellowish pigment.

Comment.—The long duration of the illness together with the appearance of transient paralysis, the marked mental deterioration, the absence of definite changes in the optic disks, and the presence of high blood pressure in a young person suggested that the differential diagnosis lay between cerebral arteriosclerosis, syphilis and neoplasm. Syphilis was considered improbable because of the negative serologic tests, in spite of the high cell count in the spinal fluid. Ventriculography was resorted to, and had the findings of this method been duly appraised, the diagnosis of neoplasm should likewise have been excluded.

Case 3.—S. P., aged 36, a storekeeper, who was admitted Oct. 26, 1923, and died October 31, had been ill since a year and a half previously when it was said he had had a nervous breakdown. He became depressed and inefficient, but after a short rest made a fair recovery. Seven months before admission he developed another attack of depression and had been declining slowly since. Sugar was found at that time in the urine, but the blood chemistry was normal. The basal metabolism rate was normal. More recently, examination by a neurologist disclosed evidence of mild aphasia, alexia and amnesia. Four weeks before admission he complained of numbness in the fingers of the right hand and of pain down the right side. There soon developed a right hemiparalysis with motor aphasia. At the same time he complained of headache, dizziness and noises in the head, and he vomited occasionally.

Physical Examination.—Examination on admission revealed: right hemiparalysis; motor aphasia; increase in all deep reflexes on the right side; absence of abdominal reflexes on the right side; right corneal anesthesia and left corneal hypesthesia. The blood pressure was 130 systolic, and 85 diastolic. The Wassermann reaction was negative with the spinal fluid and blood. There

was percussion tenderness over the left temporoparietal area, and early bilateral choked disk. Roentgenograms of the skull were negative. There was 0.6 per cent sugar in the urine on two examinations.

Treatment and Course.—The diagnosis of a left frontal neoplasm was made, and an exploratory craniotomy of the left frontal area was performed. No tumor was found; instead, a large area of softening was discovered over the left rolandic area. Aspiration of this area disclosed a large cavity containing blood. The patient died a few hours after the operation. The necropsy was limited to the cranium.

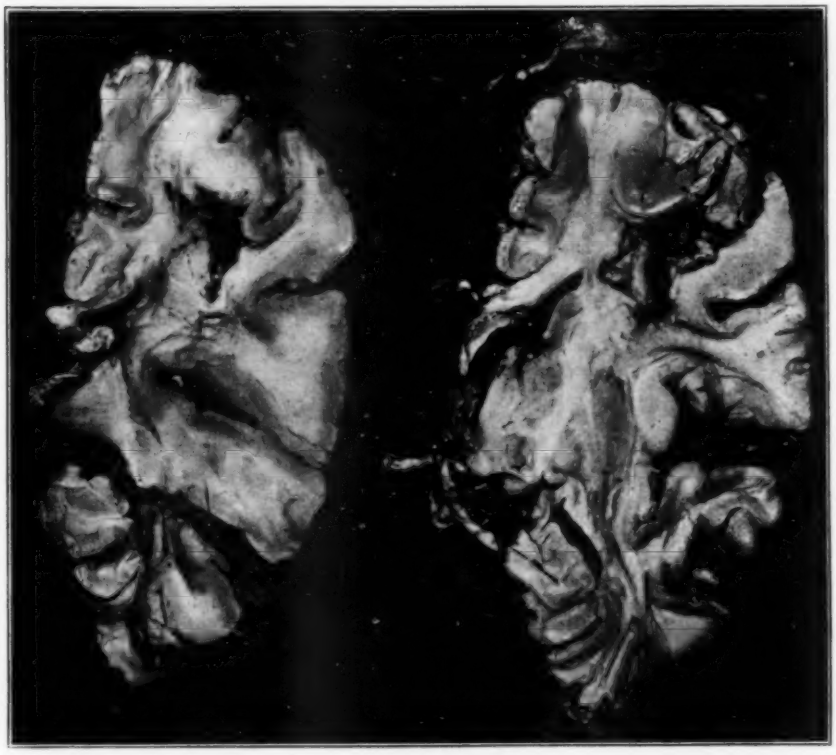

Fig. 3.—A coronal section of the brain in Case 2, showing the collapsed hemorrhagic cyst in the left frontal lobe.

Gross Anatomy.—The pia-arachnoid was somewhat dull and showed a small amount of opaque exudate along the fissures, especially over the frontal lobes. The right cerebral hemisphere showed no evidence of increased intracranial pressure. The gyri were of normal prominence and the sulci of normal depth. The left cerebral hemisphere showed an area of softening involving the posterior half of the frontal lobe and the anterior half of the parietal lobe. In this region the gyri were flattened, and the brain substance was very soft. Beneath the surface was a large cyst filled with blood and necrotic tissue. Its surface measured about 4 cm. in diameter. On incision, the wall was found to be formed by a thin layer of necrotic brain tissue. A section at the level of the genu of the corpus callosum showed only slight atrophy of the cortex

of the left cerebral hemisphere. The anterior portion of the cyst wall was first encountered in a section at the level of the anterior commissure. At this level the middle cerebral artery on the left side was much thickened, and there was a small aneurysmal dilatation of its wall. A section at the level of the mamillary bodies showed an almost complete loss of cortex in the region of the cyst (Fig. 4). The basal ganglia were swollen, and the adjacent part of the third ventricle was compressed on the left side. A small area of softening was present also in the anterior region of the hippocampus major. The right occipital lobe was normal. The left occipital lobe showed a small hemorrhagic cyst near the cortex. The cerebellum was normal.

All vessels at the base of the brain, with the exception of the left middle cerebral, were free from atherosclerotic changes. The left middle cerebral artery was markedly thickened, its lumen reduced in size, and it presented a small aneurysmal dilatation.

Microscopic Anatomy.—Numerous sections in and about the cyst and the hemorrhagic zones disclosed no inflammatory changes and no adventitial infiltrations anywhere except accumulations of phagocytic elements in the area of softening. In the area of softening, characteristic changes were found, including accumulations of granular cells with and without pigment material. In some areas necrotic foci with the character of a red infarct surrounded by a zone of reaction were found. Sections of the middle cerebral artery showed marked atherosclerotic changes in all layers and it was completely occluded by a recently formed thrombus.

Comment.—In this case it was almost impossible to differentiate on clinical grounds between a vascular insult, syphilis and neoplasm of the brain. The appearance of an early choked disk is not incompatible with the diagnosis either of arteriosclerosis or of tumor. Ventriculography offers the only possible means at our disposal for arriving at a definite conclusion in a case of this character.

Case 4.—M. S., aged 52, who was admitted March 10, 1924, and died April 16, with a past history indicative of hypertension of some duration. with occasional nosebleed and headache, became ill one week before admission, when she noticed that she could not pick up articles with her right hand as easily as usual. This was followed by flattening of the right side of her face, and a difficulty in speech consisting of inability to find certain words. She also noticed that her memory became somewhat impaired. The weakness of the right arm became more marked and spread to the right lower extremity.

Physical Examination.—On admission, the patient appeared somewhat older than her given age, poorly developed and poorly nourished. There was puffiness of the face, especially under the eyelids. The physical condition presented evidence of general arteriosclerosis and hypertension. The blood pressure was 188 systolic, and 85 diastolic.

Neurologic Examination.—The patient was apathetic, resistant, confused, somewhat disoriented and emotionally unstable; she cried and laughed on slight provocation. Her speech was impaired, and there was a mild form of so-called motor aphasia. The pupils were slightly unequal, the right larger than the left; both reacted well to light and in accommodation. There was no impairment of ocular movements, no nystagmus and no impairment of vision. There was a right hemiparesis. The deep reflexes were hyperactive, more markedly on the right side than on the left. The abdominal reflexes were not elicited. There was a definite Babinski sign on the right, but no clonus. Examination of the

ocular fundi showed the arteries to be smaller than normal and tortuous with widened veins, more marked in the left eye. The ophthalmologist made the diagnosis of arteriosclerosis. Lumbar puncture gave negative findings. Urine examination showed a few casts and few white blood corpuscles. The Wassermann reaction of the blood was negative.

At this time, the diagnosis of cerebral arteriosclerosis, with localized softening of the left motor area, was considered the most plausible, since the acute onset, rapid progression of symptoms, evidence of general arteriosclerosis, fundus changes and emotional instability were all in its favor. Tumor was excluded on these same grounds, and cerebral syphilis was ruled out by the negative serologic findings.

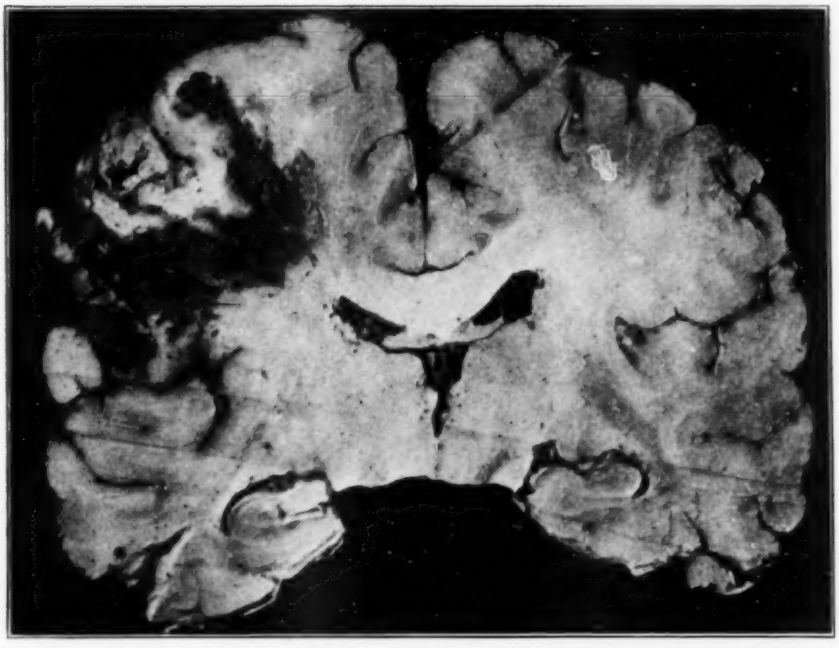

Fig. 4.—A coronal section of the brain in Case 3, showing the area of softening and a small hemorrhagic cyst.

Course.—The first days of the patient's residence in the hospital were marked by fluctuations in the mental state, and by only slight progression in the paresis. But frequent and careful examination of the eyegrounds disclosed later a slow, progressive swelling of the optic disks. Three weeks after admission, slightly blurred margins gave place to definite swelling of the optic disks. This condition was still considered by the opthalmologist to be a neuroretinitis of arteriosclerotic origin. A few days later, however, retinal hemorrhage appeared, and on April 2, the swelling of the disk measured 5 diopters.

Ventriculography was then carried out and led to the following conclusion: no air entered the lateral ventricle from the right. This suggested that there was a deep tumor on the left side in the temporal lobe pressing on the left foramen of Monro. Craniotomy, with partial excision of a tumor in the left cerebral hemisphere was then performed. After the operation, the patient

sank rapidly and death occurred forty-eight hours later. The necropsy was limited to the cranium.

Gross Anatomy.—The brain gave evidence of increased intracranial pressure. The gyri were flattened, particularly over the left frontoparietal lobe. In this region there was a crater-like excavation, the bottom of which was filled with dark, dirty brown, friable, necrotic material in the substance of which were seen several small pearly white nodules of what appeared to be neoplastic tissue (Fig. 5). On section, this tumor mass and the surrounding necrotic zone extended from within 2 cm. of the frontal pole backward through the frontal and parietal lobes as far as the beginning of the occipital lobe. The tumor may be said to have had a conical outline, the apex directed forward and the base at the posterior limit. The tumor mass was highly vascular, hemorrhagic, fairly well circumscribed and demarcated from the surrounding highly edematous zone. In the latter area a few other small neoplastic masses were noted which apparently formed independent growth centers.

Microscopic Anatomy.—The histologic picture was that of a spongioblastoma and was characterized by the presence of numerous giant cells with grotesque nuclear arrangement and nuclear fragmentation, ependymal cystlike structures, and "rosette" formations. Necrotic changes and marked vascularity were other outstanding features in this tumor.

Comment.—This case is particularly important since the history, findings and clinical course of the disease fully justified the diagnosis of encephalomalacia on an arteriosclerotic basis. The opinion of a competent ophthalmologist lent additional support to this diagnosis, and it was only when the swelling of the optic disks reached 5 diopters and retinal hemorrhages appeared that the neurologist seriously entertained the possibility of a tumor being present. Confirmation of this opinion, and localization of the growth was obtained by ventriculography.

CASE 5.—M. R., aged 4½ years, who was admitted Dec. 18, 1920, and died Jan. 29, 1921, with a past history of measles, chicken pox, influenza and four attacks of pneumonia, had been ill since five months before, when attacks of severe headache associated with spells of vomiting suddenly developed. One month before admission the headache became more intense and was followed by dizziness and a tendency to fall to the right. The gait became unsteady; the head was inclined to the right; the appetite became poor, and rectal and vesical sphincter control became impaired. In the past week there had developed a sticking sensation in both hands. More recently, there appeared brief episodes in which the body became rigid and there were rhythmic, spasmodic muscular contractions.

Physical Examination.—The face had a masklike expression. There was no paralysis, but attacks occurred in which the whole body, trunk and extremities, was involved in rhythmic, spasmodic contractions, all muscles becoming rigid for a period of several minutes. Between these attacks the muscles were relaxed and flaccid. On standing, the patient swayed from side to side, falling to the right. The deep reflexes varied from time to time. During spasmodic contractions they were exaggerated; in the free interval they were diminished. They were equal on the two sides in both instances. There was no Babinski sign. Adiadokokinesis was present on the right side. There was bilateral papilledema with 6 diopters elevation. Sphincteric control was lost.

Course.—The findings suggested a cerebellar neoplasm, and suboccipital decompression with exploration was carried out, but no neoplasm was found.

Following the operation there was a rapid rise in temperature, and a rapid decline in the general condition of the patient. Death occurred four days after the operation, and the case was considered to be one of acute epidemic encephalitis. The necropsy was limited to the cranium.

Gross Anatomy.—There was a large suboccipital decompression exposing the entire cerebellum. The left cerebellar lobe was large and badly macerated, friable and excavated by a cyst filled with blood. At the lower edge of the cyst a medium sized vessel was exposed which showed aneurysmal dilatation (Fig. 6).

Microscopic Anatomy.—In the cerebellum, adjacent to the hemorrhagic cyst, were numerous newly-formed blood vessels, and many hemorrhages. Several

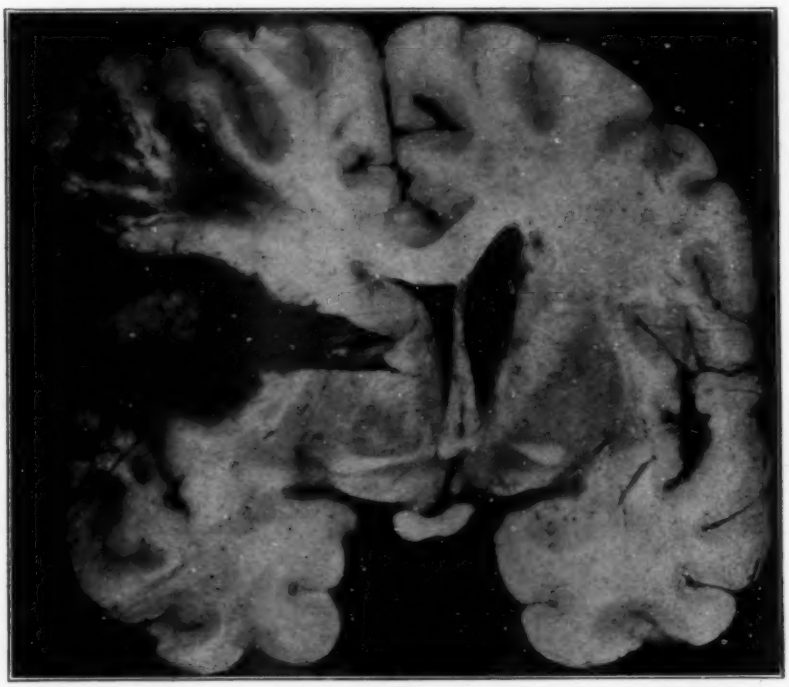

Fig. 5.—A coronal section of the brain in Case 4, showing the highly vascular tumor mass.

cystlike structures, with changes strongly suggestive of recent glial reactions, were found in the tissue adjacent to the hemorrhagic area.

Case 6.—M. R., aged 13, who was admitted Aug. 30, 1924, and died August 31, with a past history of measles, pertussis, tonsillitis and laryngitis, had apparently been ill for about three weeks, when she complained of a feeling of general weakness. While at the theater, she suddenly became dizzy and, on the way home, fell, but was caught before touching the ground. She soon lost consciousness and was brought to the hospital in a stuporous condition. Occasionally she would mutter, "My head aches."

Physical Examination.—There were no signs of injury. The patient was comatose; pressure on the supra-orbital nerve caused an expression of pain on

the face. The right pupil contracted sluggishly to light. There was slight stiffness of the neck, and a slight bilateral Kernig sign. The deep reflexes were not elicited; the abdominal reflexes were absent, except the left lower reflex, which was diminished; there was a Babinski sign on both sides. The cerebrospinal fluid was under increased pressure and "bloody" (the blood apparently not traumatic in origin). The blood pressure was 110 systolic, and 60 diastolic.

Course.—On the following day the condition remained unchanged except for conjugate deviation of the eyeballs to the right, right facial weakness and bilateral corneal hypesthesia. The ocular fundi were negative. The urine findings were negative. A provisional diagnosis was made of hemorrhage into a gliomatous cyst or neoplasm. The patient sank rapidly and died twenty-four hours after admission to the hospital. The necropsy was limited to the cranium.

Gross Anatomy.—On the right side of the skull in the anterior parietal region there was a marked elevation, somewhat conical in shape, apparently due to exostosis of the external table, the internal table in the same location showing a corresponding funnel-shaped depression. The dura was adherent in this location. The underlying pia-arachnoid was somewhat thickened and opaque. The cerebral hemispheres, aside from slight evidence of increased intracranial pressure, were normal in appearance. The left lenticular nucleus and adjacent posterior limb of the internal capsule contained two small, irregular, cystlike openings having smooth inner walls, measuring about 4 mm. in diameter and extending throughout the entire depth of these structures (Fig. 8). The vessels in the substance of the brain were rather prominent, but no definite sclerotic changes were obvious to the naked eye.

The right cerebellar hemisphere was increased in size, the vessels overlying it being markedly congested; the cerebellar structure was apparently swollen, and fluctuated on palpation. On incision a recent hemorrhagic focus was seen, measuring about 1.5 cm. in diameter and occupying the posterior half of the white substance (Fig. 7). The overlying cortex was markedly edematous and swollen. Both conditions caused displacement of the right superior cerebellar peduncle and narrowing of the fourth ventricle. The cerebellar cortex overlying the hemorrhage was dirty gray and apparently necrotic. The major portion of the dentate nucleus was involved in the hemorrhagic and in the softening process. The hemorrhage was dark red in its dependent portion, but in its anterior superior half was grayish red and granular.

Microscopic Anatomy.—Sections through the cyst formations in the basal ganglia showed that the process was acute and destructive in nature, probably as a result of closure of a blood vessel in the vicinity, with secondary ischemic softening. Several vessels in the vicinity of the areas of softening presented fairly typical infiltrations with granular cells and lymphocytes. A section taken in the vicinity of the hemorrhage in the cerebellum presented the picture of softening, but no evidence of tumor formation or inflammatory changes.

Comment.—The history and symptoms presented by this case and Case 5 permit only the diagnosis of tumor cerebelli. At the age of these patients, arteriosclerosis does not enter into consideration, and there was no evidence of an inflammatory process, though the possibility of epidemic encephalitis was considered. There was likewise no history of trauma to suggest the presence of a hemorrhagic lesion. These cases must be considered as belonging to the rare group in which there is an inherent defect of the blood vessels leading to hemorrhage in early life. Such conditions are known to occur in persons with

status lymphaticus. It is also possible that the hemorrhages were due to rupture of small mycotic aneurisms.

Case 7.—I. S., aged 59, who was admitted June 12, 1924, and died June 21, had had seven children most of whom had had frequent nose bleed. Thirty years before admission, at the age of 27, for a period of two years the patient had a few infrequent, so-called epileptic attacks. At the end of this period

Fig. 6.—Basal surface of the brain in Case 5. The fusiform aneurysmal dilatation of vessels with cavitation in the left cerebellar hemisphere may be noted.

she remained free from such attacks until two years before admission when there was a return of the seizures; these had since recurred at the rate of one attack every three or four months. For the past twenty-five years the patient also suffered with kidney trouble, which developed in the course of childbirth. At that time she was acutely ill for five or six weeks, passed bloody urine, had

swollen feet and a period of unconsciousness. The patient also had had frequent nose bleed. The present illness dated from two months before admission, when the so-called epileptic attacks became frequent, occurring from one to four times weekly. The convulsive seizures were described as sudden in onset; the patient fell to the ground, the body became rigid and shook, the eyes were glassy, the face was cyanotic, and froth appeared at the mouth. The attacks lasted for about twenty minutes, at the end of which the patient appeared dazed

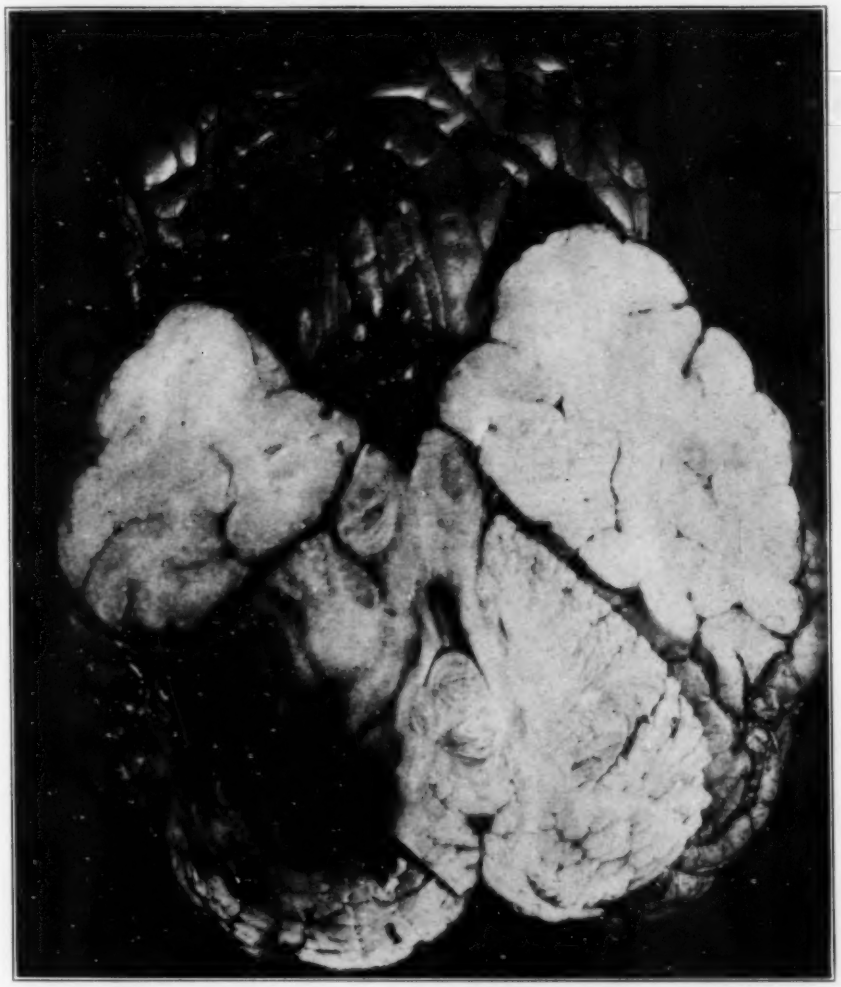

Fig. 7.—Hemorrhagic focus in the left cerebellar hemisphere in Case 6.

and complained of severe pain in the back of the head. For the last twenty-four hours the attacks had become still more frequent, occurring almost every half hour. Between attacks the patient was in a stupor and could be aroused only with difficulty. There was no history of vomiting, chills or rise in temperature.

Physical Examination.—The patient was in coma; no uremic odor was detected. The pupils were unequal, the left dilated and fixed, the right con-

tracted and reacting very sluggishly. Convulsive attacks occurred every half hour. They were of jacksonian character. The twitchings began on the left side of the face and spread to the arm and leg of the same side and then to the right side. The contractions were clonic in character, and more marked on the left side than on the right. Lumbar puncture gave a clear fluid under increased pressure, containing a few red blood cells. The blood pressure was 140 systolic,

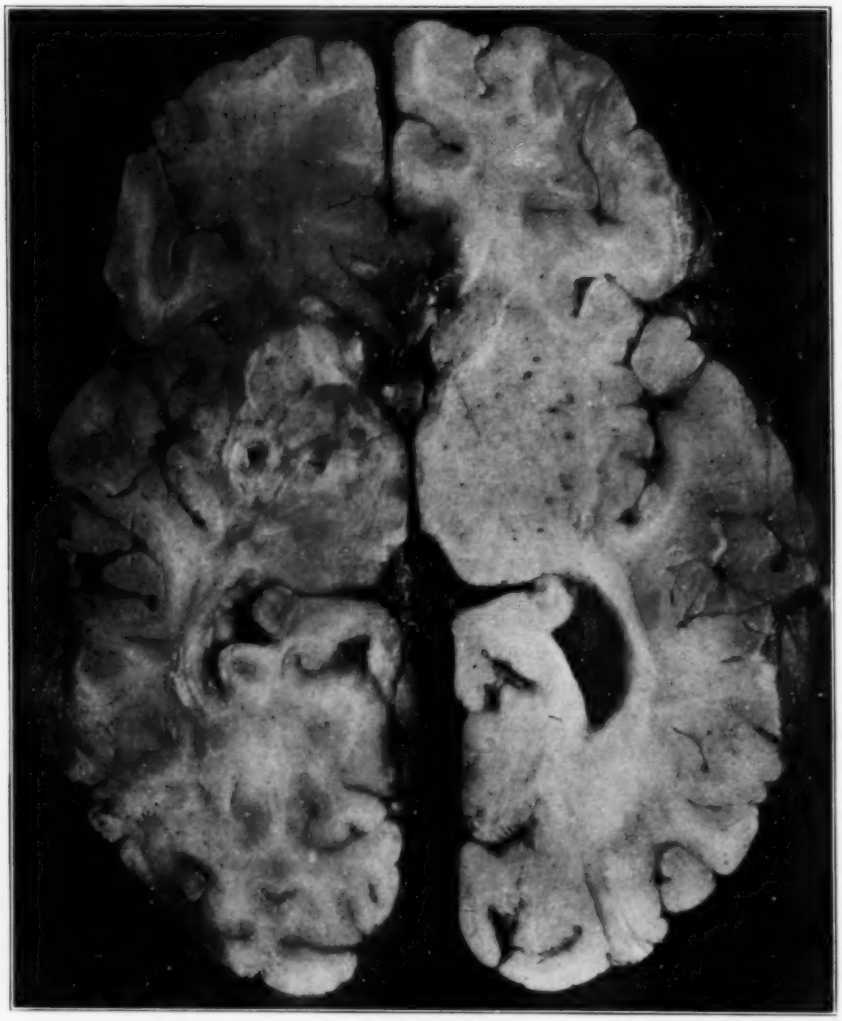

Fig. 8.—Distention of ventricle, and cystic areas in the left corpus striatum in Case 6.

and 77 diastolic. There was apparently no loss of motor power; all deep reflexes were very active, on the left more than on the right; the abdominal reflexes were absent; the Babinski sign was present on both sides. The left optic disk had a clear margin and marked pallor; the vessels were thin walled and not tortuous. The laboratory findings were as follows: blood Wassermann

reaction, negative; blood chemistry—urea nitrogen, 23.1; noncoagulable nitrogen, 51; uric acid, 31; creatinin, 1.1. The diagnosis made at this time was essential epilepsy and status epilepticus. Large doses of chloral and phenobarbital did not, however, control the epileptiform attacks.

Clinical Course.—For the first few days in the hospital some improvement was noted; the patient became more alert and cooperated better. There was then a definite left hemiparesis and left Babinski sign and the left pupil was large and fixed. Convulsions still occurred, though less frequently, but were of longer duration; they were more marked on the left side. Encephalitis or multiple neoplasms were considered in diagnosis.

June 14, it was noticed that the patient's condition was becoming worse. The convulsive seizures had again become more frequent. They were preceded by vertigo and would begin in the left side of the face, the mouth being drawn to the left; the eyes turned to the left, the left eyelids were closed, the left arm flexed slowly, and simultaneously the left leg began to flex. With this there was no complete loss of consciousness; the patient could remember questions asked during the attack. Directly after an attack, the left hemiparesis was more marked. The frequency of such attacks, the jacksonian character and the fairly good localizing signs pointed to a right frontal lesion. A roentgen-ray examination showed marked dilatation of the right anterior diploic veins merging into a calcareous mass lying in front of the motor area.

June 20, an exploratory craniotomy was done, and several tumor masses were found on the surface of the cortex, each globular in appearance and enveloped by a thick capsule; another small mass could be felt in the depth of the brain substance.

The patient died, June 21, twenty-four hours after the operation. The necropsy was limited to the cranium.

Gross Anatomy.—The brain was taken out in pieces so that no detailed observation as to its form could be made. Aside from some flattening of the gyri in areas outside the diseased portion of the brain, and a moderate amount of atheromatous changes in the vessels, no striking changes were noted. The area involved in the disease process was the right frontal lobe, which was definitely smaller in size than the corresponding portion of the other hemisphere; the gyri were atrophic and thrown into supernumerary folds. On the surface near the dorsal border (Fig. 9), there was a large vessel growing forward and parallel to the dorsal border and terminating in a small sac about 1 cm. in diameter. The sac was embedded in a depression about 5 cm. posterior to the frontal pole. On elevating the sac a depression was found, lined by smooth and glistening pia. Directly posterior to the sac there was another elevation measuring on the free surface about 1.5 cm. in diameter. On cutting into the brain at this point, another larger, encapsulated mass was revealed. This was oval in outline, measured 3 cm. in the long diameter, and was embedded deep in the substance of the frontal lobe. A cut section of this mass (Fig. 10) showed it to be hard, somewhat brittle, grayish-brown, and giving the impression of an organized thrombus in an aneurysmal cyst. Directly posterior to this, extending back as far as the postcentral gyrus, there were several similar cysts varying in size from 0.5 to 2 cm. in diameter. The smaller cysts were also well encapsulated, surrounded by thick, fibrous, calcified walls. Their cavities were filled with yellowish, granular material and a small amount of yellowish fluid; the inner lining of the walls, however, was smooth, grayish white and glistening. All the cysts were easily dislodged from the substance of the brain, leaving behind smooth surfaces of only moderately softened brain

substance. All these cystic structures gave the impression of being aneurysmal dilatations of calcified vessels, though only one, the most anterior cyst, could be traced to a vessel, the wall of which appeared to be continuous with that of the cyst.

Microscopic Anatomy.—Cross section through the aneurysmal sacs and adjacent cerebral cortex showed that the wall of the sacs had retained some of the histologic features of a medium-sized vessel wall with its division into adventitia, media and a markedly distorted intima. The last was fused with a highly organized thrombus which had undergone canalization. The nerve

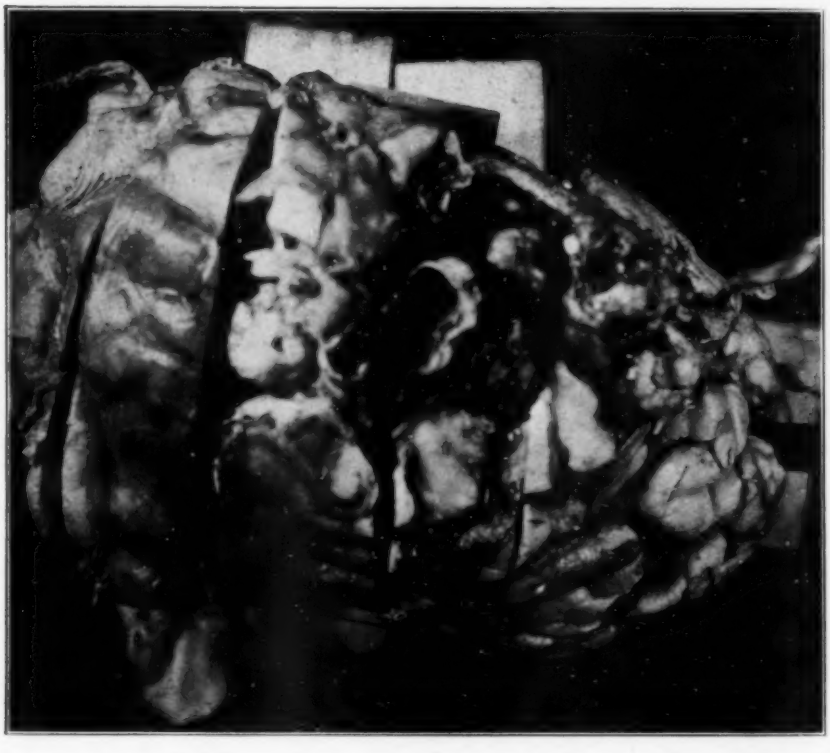

Fig. 9.—Calcified aneurysmal cysts and calcified vessel near the dorsal border in Case 7.

tissue adjacent to the aneurysms showed evidence of softening, and mild infiltrative changes with small round cells, apparently a reactive change.

Comment.—While this turned out to be a case of vascular disease, the aneurysms found at the operation could be considered as acting like tumors in the production of symptoms, so that a differential diagnosis between these two conditions was impossible. The case is interesting both because of the rarity of the condition, and because of the clinical history. It is possible that the early epileptic seizures were due to the formation of the aneurysmal dilatation of the vessels, and that the brain adjusted itself to the presence of these foreign bodies, with a consequent cessation of epileptic phenomena. As the

patient became older, changes unquestionably took place in the blood vessels and nutrition of the brain substance, and the aneurysms began again to act as irritative foci, with consequent recurrence of epileptic attacks. We can assume that the balance of equilibrium of the brain function was disturbed not merely by the presence of the aneurysms but rather by the degenerative changes associated with advancing years.

Fig. 10.—Cross sections of the aneurysmal cysts in Case 7. The relation of the main cyst to the overlying blood vessel may be noted.

SUMMARY AND CONCLUSIONS

A survey of the clinical features in our cases indicates that sufficient justification was present in every instance to consider the diagnosis of brain neoplasm. This is particularly true of those cases in which cerebellar localization was apparent and later verified. In every instance

there were present one or more of the symptoms of brain tumor. Definite choking of the disks was present to a marked degree in two of the three cases, Cases 1 and 5, with cerebellar localization. In only one case, Case 6, with similar localization of the lesion was there no change in the disks, very likely because of the brief course of the illness.

On the other hand, in the remaining three cases disk changes were less constant and much less marked in degree. Thus in only one, Case 3, was there evidence of early bilateral papilledema. In another, Case 7, contralateral postneuritic atrophy is recorded, while in still another, Case 2, marked engorgement of the veins on the homolateral side was the only fundus finding. It is remarkable that no arteriosclerotic fundus changes were found in any case but one, Case 1, in which the latter condition was overshadowed by later development of a high degree of papilledema.

Headache, vomiting and dizziness were prominent symptoms mainly in the cases with cerebellar localization, probably because of the internal hydrocephalus incident to cerebellar lesions. On the other hand, in instances with cerebral involvement the outstanding features were the more protracted clinical course, the early appearance of intellectual defects and of emotional instability, and more pronounced paretic phenomena.

The quite striking divergence in the clinical pictures manifested by vascular lesions in these two main locations, while in many ways in full accord with the generally recognized difference existing between neoplastic lesions in similar localizations, is explained, in our opinion, by the action of the lesion on the ventricular system. Supratentorial vascular lesions are destructive and do not influence the form and shape of the ventricles. In the cases of subtentorial vascular lesion, there occurred a moderate internal hydrocephalus due to compression of the fourth ventricle. This action is probably due to encroachment on the unprotected roof of this ventricle and the adjacent part of the aqueduct of Sylvius. The internal hydrocephalus in these cases renders ventriculography of little aid in diagnosis as to the nature of the lesion, unless the hydrocephalus is extreme.

The question now arises as to what may be found in the clinical histories and course of the cases cited that would enable one to establish the true character of the process. We have reached the conclusion that vascular lesions simulating tumors of the brain can be put into two main groups with transitional forms.

In one group, Cases 1, 2 and 3, the cerebral lesion is simply an additional expression of an acquired "vascular" damage, which has developed in the course of some generalized disease, such as syphilis, diabetes, arteriosclerosis, cardiorenal disease, etc.

In another group, Cases 5 and 6, the vascular lesion of the brain is the result of an inherent (discrasic) defect in the vascular system, as seen in the status thymicolymphaticus.

In the transitional group, Case 7, both factors, inherent and acquired, cooperate to give rise to a lesion of complex and unusual form.

This grouping will be found of service when it is realized that we have no direct method for a strict separation of lesions of the brain into neoplastic and vascular groups, and that indirect evidence is our only guide for such a distinction in many instances. It is quite apparent that vascular lesions of the brain (aneurysms, cysts, etc.) may give rise to some or all of the cardinal symptoms of brain neoplasm. In spite of the dominating cerebral symptoms, evidence outside the central nervous system must be sought, analyzed and weighed before we take any radical therapeutic steps based purely on neurologic signs. Even after having exhausted all these indirect diagnostic means, there are still times when the diagnosis remains uncertain; then ventriculography is of great advantage and, in spite of its dangers, should be employed. It was utilized in Case 4 and other similar cases in which the abrupt onset, the clinical picture in the early phase of the illness and the objective findings led to the diagnosis of cerebral thrombosis. Only late in the clinical course, after papilledema had appeared and developed rapidly into a high degree of choking of the disks, was tumor cerebri suspected. Ventriculography then disclosed a deformity of the ventricular cavity on the side involved and established the presence of a neoplasm. The tumor was found to present the gross and microscopic features of a "spongioblastoma," [1] whose malignant qualities and clinical manifestations make it almost indistinguishable from vascular lesions of the brain. Frequently, in our opinion, it can be identified during the life of the patient only with the aid of ventriculography. Case 2 presents a clinical picture almost parallel to that of Case 7, and yet presents not only a striking contrast in anatomic lesion, but also in ventriculographic picture—the latter, in our opinion, being sufficient to contraindicate craniotomy.

1. Globus, J. H., and Strauss, Israel: Spongioblastoma Multiforme, Primary Malignant Form of Brain Neoplasm; Its Clinical and Anatomic Features, Arch. Neurol. & Psychiat. **14**:139 (Aug.) 1925.

STUDIES OF CASTS OF THE CEREBRAL VENTRICLES *

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The advent of the pneumoventriculogram has made it imperative that we have a clear mental picture of the contour of the normal cerebral ventricles. Studies to this end which formerly would have had merely an academic interest become now of direct practical value.

During the past year, in collaboration with Dr. Naffziger, an attempt has been made to supply a satisfactory visualization of the cerebral subarachnoid spaces.[1] Celloidin casts were made for this purpose. For the present study similar casts of the cerebral ventricles have been made. In six out of fifteen injections, the casts were sufficiently complete to warrant careful study.

PREPARATION OF CASTS

The mass employed for the injection was a celloidin acetone camphor mixture. On account of the great viscosity of the injection mass pressures of from 200 to 400 mm. of mercury were required. Fresh human cadavers were used. After the necessary perforations of the skull, ventricle needles were inserted into each lateral ventricle, and the cerebrospinal fluid was entirely removed by repeated through and through irrigation with acetone. The injection mass was then introduced through one needle, allowing the residual acetone to be expelled from the second needle which was then plugged by its stylet. The injection was continued for twenty-four hours, since, as the loss of acetone caused the injection mass to solidify, the celloidin had a tendency to contract. A prolonged injection was therefore required to make up for this shrinkage. After the injection was completed, the head of the cadaver was placed in cold water for twenty-four hours and then immersed in commercial hydrochloric acid. The action of the acid removed the muscles, cranium and dura but, of course, had no action on the celloidin cast. A certain amount of brain tissue, the high fat content of which caused it to remain undigested by the acid, was removed by repeated washing.

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* From the Division of Neurological Surgery, Cleveland Clinic.

* Read before the Section on Nervous and Mental Diseases at the Seventy-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., May, 1925.

1. Locke, C. E., and Naffziger, H. C.: The Cerebral Subarachnoid System, Arch. Neurol. & Psychiat. **12**:411-418 (Oct.) 1924.

STUDY OF THE CASTS

The lateral view of the ventricles (Fig. 1) is one with which we are familiar, and thus the casts viewed from this angle give no new conception.

The vertical aspect of the cast from above, however, is most instructive. We have the habit of visualizing the ventricles in profile, and it is not until they are studied from above that we realize that each lateral ventricle does not lie in a single sagittal plane. In Figure 2, it will be noted that the anterior horns of the lateral ventricles approximate each other closely throughout a considerable area while the posterior horns are widely separated. The tips of the anterior horns are

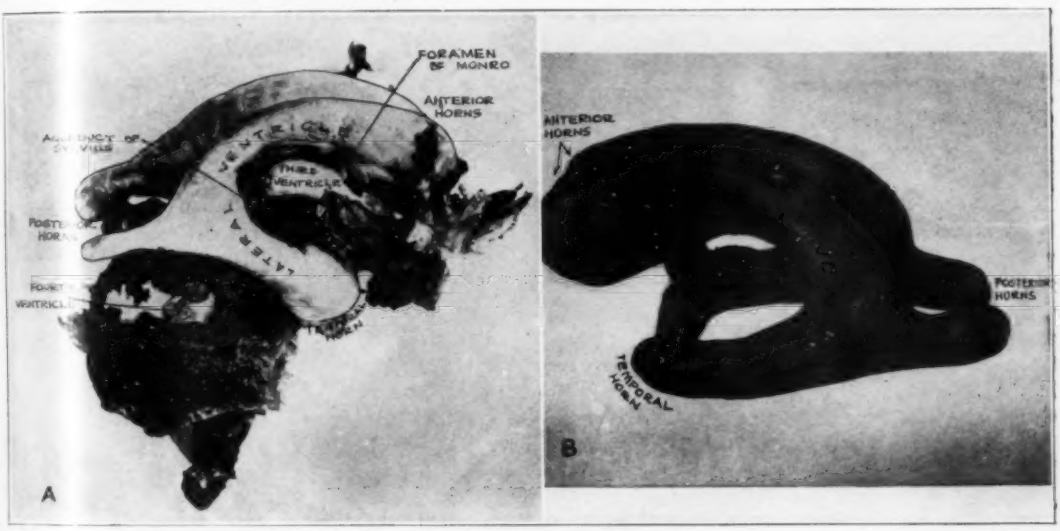

Fig. 1.—*A*, celloidin cast of cerebral ventricles and subarachnoid spaces (lateral view); *B*, wax model of cerebral ventricles.

slightly separated from each other. As they extend posteriorly, however, they lie in close proximity to each other for a considerable distance. In a region just anterior to the bodies of the lateral ventricles there is an abrupt divergence from the midsagittal plane. As the anterior horns join the bodies of the lateral ventricles this divergence is still maintained, so that the right and left lateral ventricles in this region are separated by several centimeters. It is not until the posterior horns are reached that the ventricles again tend slightly toward each other.

It is interesting to note that the maximum lateral extension of each ventricle is in the region of the middle third of the inferior horn. As

soon as the points of maximum lateral extension are reached, however, the inferior horn takes a sharp turn toward the midline, so that it again approaches the sagittal plane of the anterior horns.

The anterior and posterior aspects of the casts are of interest in that they are in accordance with the points which have been noted in studying the vertical aspects. Figures 3 and 4 demonstrate the close apposition of the anterior horns, the separation of the posterior horns and the changes in the direction of the curves of the temporal horns.

INTERPRETATION OF VENTRICULOGRAMS

A study of the ventricular casts has led us to conclude that the anterior-posterior and posterior-anterior ventriculograms are of major

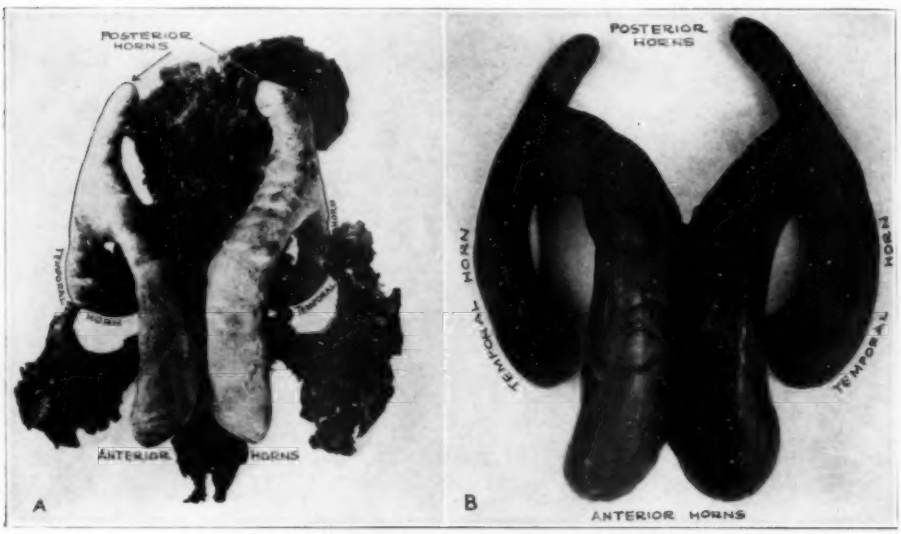

Fig. 2.—*A*, celloidin cast of cerebral ventricles and subarachnoid spaces (vertical view from above); *B*, wax model of cerebral ventricles (vertical view from above).

importance. The lateral ventricle shows so much variation in the frontal plane that frontal sections through different portions of the ventricle casts can be identified easily by the contour of the cut surfaces. If we are familiar with the appearance of air in different portions of the lateral ventricle, we may readily recognize ventricle displacements or obliterations in anterior-posterior and posterior-anterior ventriculograms. Since ventricular displacements occur more frequently in the frontal plane, these views are especially serviceable for demonstrating them. Obliterations are accurately shown when the air fails to pass freely to the highest level when the position of the head is altered.

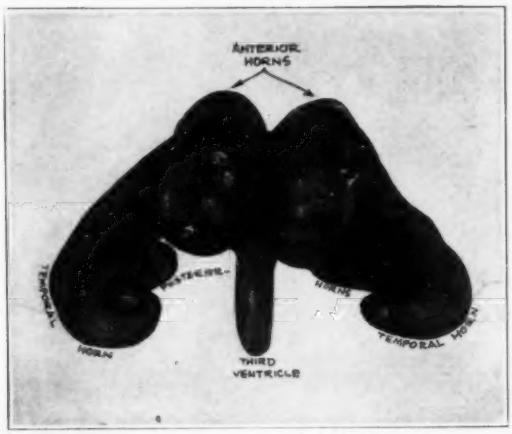

Fig. 3.—Wax model of cerebral ventricles (anterior view).

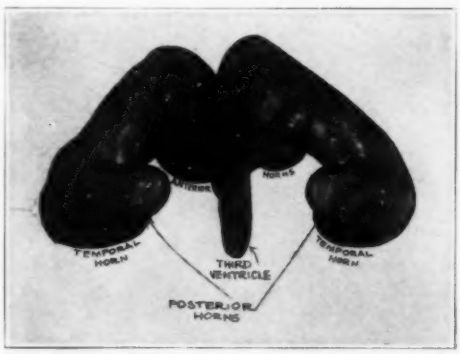

Fig. 4.—Wax model of cerebral ventricles (posterior view).

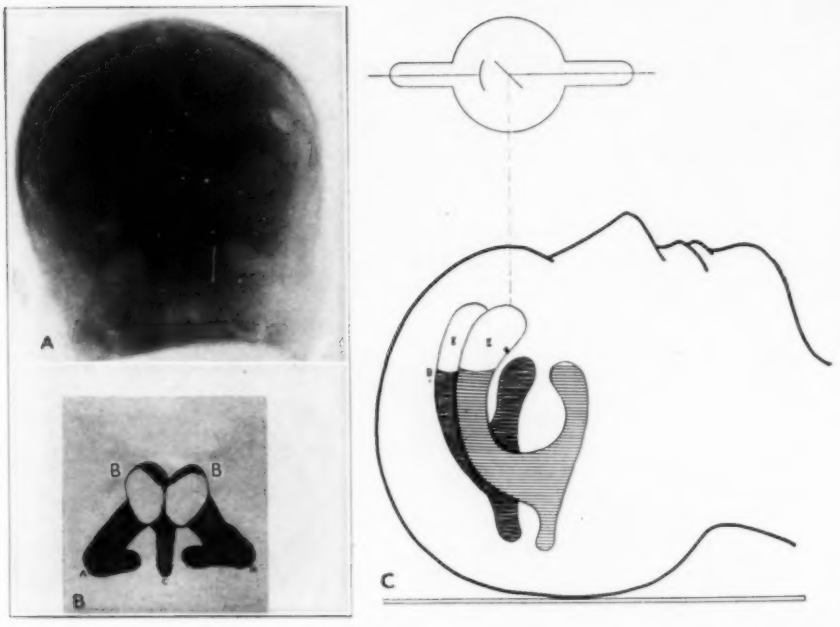

Fig. 5.—*A*, anterior-posterior ventriculogram; *B*, wax cast of ventricle cut in plane to correspond with the separation of air and fluid in the ventriculogram; *C*, position of head when ventriculogram was taken and position of air in ventricles; *a*, temporal horns; *b*, anterior horns; *c*, third ventricle; *d*, fluid level; *e*, air.

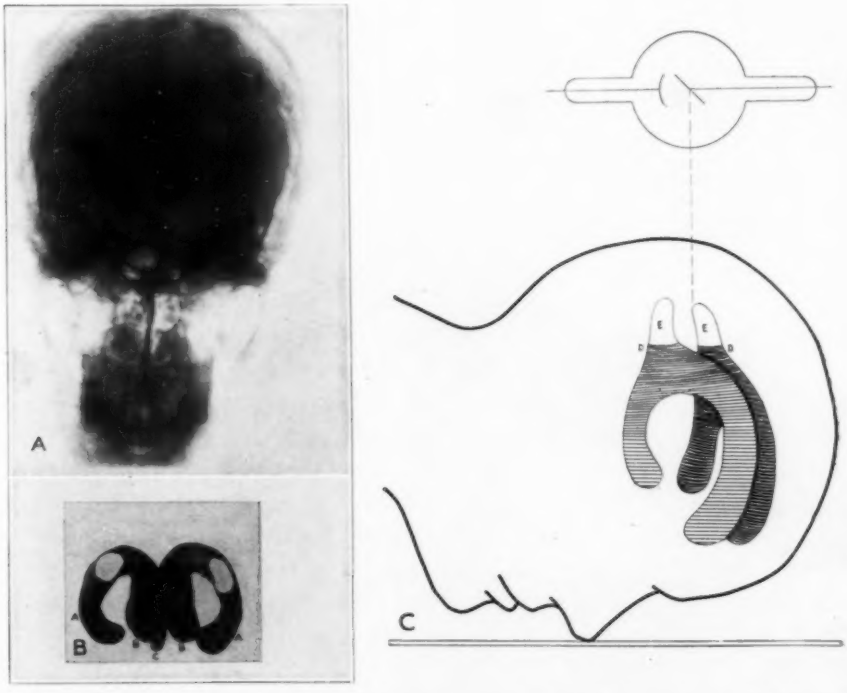

Fig. 6.—*A*, posterior-anterior ventriculogram; *B*, wax cast of ventricle cut in plane to correspond with the separation of air and fluid in the ventriculogram; *C*, position of head when ventriculogram was taken and position of air in ventricles; *a*, temporal horns; *b*, anterior horns; *c*, third ventricle; *d*, fluid level; *e*, air.

For illustrative purposes we have had our celloidin casts of the ventricles reproduced in wax, in order that they may be easily cut in various planes. In Figures 5, 6 and 7, these waxen casts of the ventricles have been sectioned in planes, each of which corresponds with the fluid level of the cerebrospinal fluid in the ventricle of the ventriculogram which accompanies it.

Figure 5, *A*, is an anterior-posterior ventriculogram. Because of the juxtaposition of the lateral ventricles, it can be seen at a glance, by reference to Figure 2, that the air is in the anterior horns, for it is only in this region that the ventricles lie so close together. The diagram

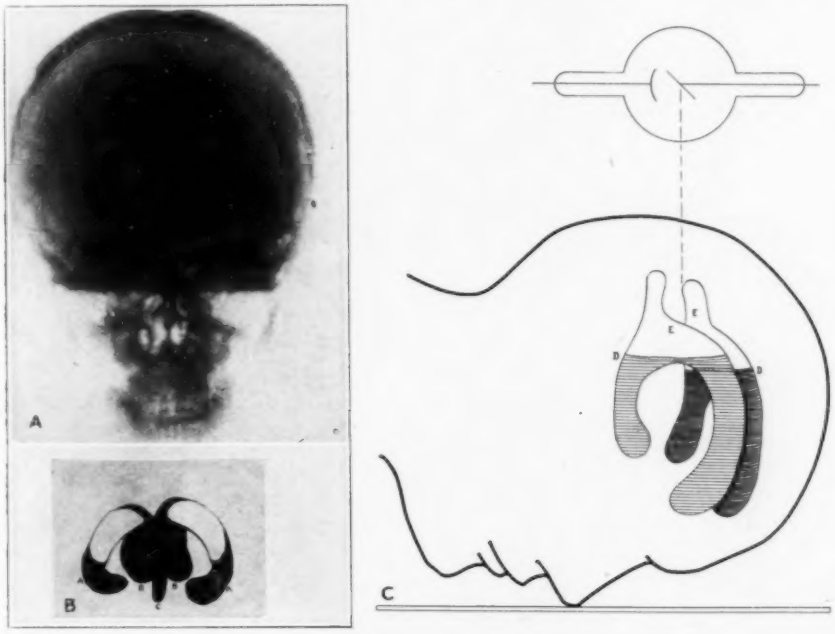

Fig. 7.—*A*, posterior anterior ventriculogram; *B*, wax cast of ventricle cut in plane to correspond with the separation of air and fluid in the ventriculogram; *C*, position of head when ventriculogram was taken and position of air in ventricles; *a*, temporal horns; *b*, anterior horns; *c*, third ventricle; *d*, fluid level; *e*, air.

in Figure 5, *C*, shows the position of the head, as well as the position of the air in the ventricles when the roentgenogram was taken. Figure 5, *B*, shows a waxen cast of the ventricle cut in a plane which corresponds to the level of the separation of the air and fluid in the ventriculogram.

Figure 6, *A*, is a posterior-anterior view. The wide separation of the air in the left and right ventricles makes it certain that it is in the posterior horns. Figure 6, *C*, illustrates the position of the head when

the foregoing view was taken, and the location of the air. Figure 6, *B*, shows a ventricle cast cut in the same plane as the fluid level in the preceding ventriculogram.

Figure 7, *A*, is a posterior-anterior film of the ventricles which contain more air than those shown in Figure 5. In this case, sufficient air was injected to fill the bodies, as well as the posterior horns of the lateral

Fig. 8.—Anterior-posterior ventriculogram showing displacement toward the midline and downward of the left lateral ventricle by an overlying tumor.

ventricles. This accounts for the divergence of the ventricles from above downward, as it appears in the ventriculogram. It is evident that there is no air in the anterior horns, for the ventricles do not sufficiently approach each other. The accompanying diagram, Figure 7, *B*, and the casts of the ventricles shown in Figure 7, *C*, further illustrate these films.

The importance of the anterior-posterior and posterior-anterior ventriculograms cannot be overestimated. If we clearly recognize the appearance of the casts of the ventricles as they appear when viewed from above, and of the air in the different portions of the lateral ventricles as shown in Figures 5, 6 and 7, the anterior-posterior and posterior-anterior ventriculograms become of invaluable assistance in the detection of displacements and obliterations of the ventricles.

Figure 8 is an anterior-posterior ventriculogram in which an overlying neoplasm has caused a displacement mesially and inferiorly in the region of the body of the left lateral ventricle.

Figure 9, *A*, is an anterior-posterior ventriculogram which illustrates the obliteration of the right anterior horn by a tumor in the

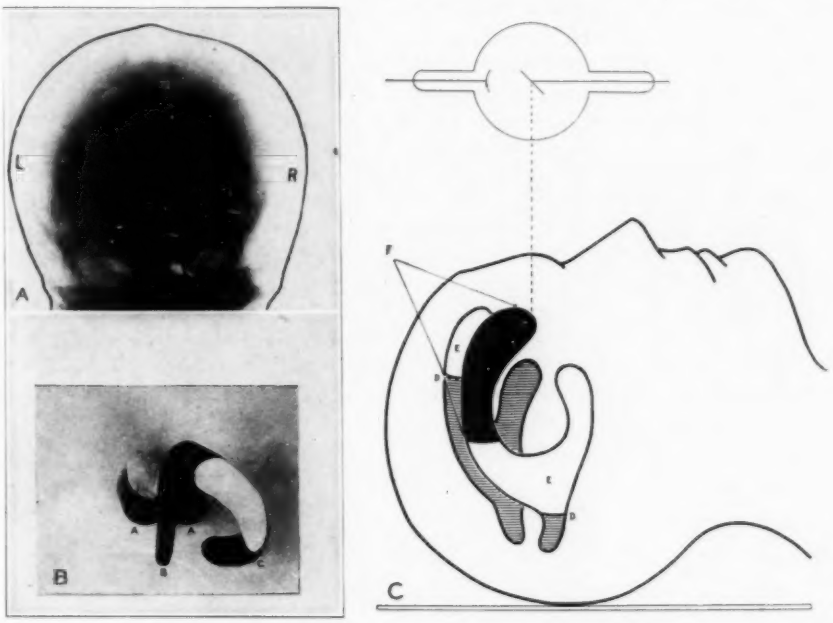

Fig. 9.—*A*, anterior-posterior ventriculogram retouched; *B*, wax cast of ventricle cut in plane to correspond with the separation of air and fluid in the ventriculogram; *C*, position of head when ventriculogram was taken and position of air in ventricles; *a*, anterior horns; *b*, third ventricle; *c*, temporal horn; *d*, fluid level; *e*, air; *f*, obliterated by neighboring neoplasm.

right frontal region. The diagram in Figure 9, *B*, shows the position of the head when a lateral radiogram was taken, as well as the position of the air in the ventricle. A wax cast of the ventricle sectioned in planes corresponding to the level of the fluid in the right and left lateral ventricles is shown in Figure 9, *C*. It is evident that the air in the left ventricle reached the tip of the anterior horn without obstruction. The air in the right ventricle, however, has been prevented from reaching the anterior horn and remains in the body of the ventricle.

CONCLUSIONS

1. A study of casts of the cerebral ventricles, especially of their vertical aspects, is a valuable aid in the interpretation of ventriculograms.

2. The value of the anterior-posterior and posterior-anterior ventriculograms should be emphasized. They require the injection of less air than is needed for the lateral films, thereby reducing the danger of the procedure. They are more efficient for the demonstration of displacements of the ventricles, and they satisfactorily demonstrate obliteration of the ventricles.

DISCUSSION

Dr. Charles H. Frazier, Philadelphia: There is no doubt that we must devise some means of lessening the risk of the ventriculography. In a collection of 182 cases made by Dr. Francis Grant, the mortality throughout the country was estimated at about 10 per cent. That is a high mortality for a diagnostic method, so that any proposal which eliminates the risk of the procedure itself to a certain extent is most acceptable. We must learn, too, to be able to interpret with greater exactness the shadows as they are shown in the roentgenogram, and one of the ways in which we can learn how to interpret them has been demonstrated by Dr. Locke. I was very much impressed a few weeks ago in New York by a series of casts of ventricles constructed by Dr. Silbert under Dr. Elsberg's direction. Two very interesting points were brought out. One was the determination as to laterality in cases in which there is uncertainty as to whether the tumor may be in the right or left hemisphere. Another point demonstrated by Dr. Silbert had to do with tumors of the posterior fossa; when in doubt as to whether the tumor occupies the right or left hemisphere, it will be found that the posterior horn of the lateral ventricle does not extend as far posteriorly on the side of the tumor as it does on the opposite side.

THE CONSTANT RELATION BETWEEN POSTURES OF MOTILE AND RIGID STATES*

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NEW YORK

I. Introduction.

II. Grouping of Stereotyped Movements and Postures.

III. Factors Preventing the Appearance of Stereotyped Movements and Postures.

IV. The Relation of Stereotyped Postures to the Stereotyped Movements in Which They May Occur.

(*a*) Movements from Positions of Rest.

(*b*) Postures Occurring in Repeated Stereotyped Movements (walking).

V. Summary.

VI. Literature.

INTRODUCTION

My purpose is to simplify our knowledge of various stereotyped postures and movements by showing that both can be easily grouped, that the muscles underlying the posture element in stereotyped motile states correspond precisely to those underlying the posture element in the corresponding stereotyped rigid states, and that a constant relation exists between these two posture groups.

The question of kinetic and tonic innervation requires a short consideration. It is universally admitted that the muscles are activated in both ways. It has been shown recently by Cobb[1] that, considered electromyographically, these two types of innervation, as Hughlings Jackson said of tremor and rigidity, "differ not fundamentally but in degree." They differ only in "continuity and duration." Further, "Voluntary muscular contractions, clonic and tonic convulsive contractions, phasic reflexes and postural reflexes are all tetanic in character."

Impulses that activate postures may be likened to the electric current that passes to a large electric sign. When the impulses reach the sign, they are distributed to a number of electric light bulbs linked by wires to make a design or pattern. It is the arrangement of the wires connecting the bulbs that determines this pattern. To carry the analogy further, the electric current activates the pattern, and the wiring of the bulbs determines the variety of the pattern. In a similar manner, the activating impulses of the nervous system pass to a mechanism that determines which muscles shall be in action and which shall not, and thus determines the muscular patterns of posture. Activation is the process underlying "whether a posture shall be"; it initiates and con-

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* Read by title at the Fifty-First Meeting of the American Neurological Association, May 5, 1925.

1. Cobb, S.: Electromyographic Studies of Experimental Convulsions, Brain **47**:70 (Feb.) 1924.

tinues muscle activity. Determination is the process underlying "what a posture shall be"; it correlates and integrates muscle activity. Therefore, as a starting point in considering the relations of motile and rigid states, there are two types of closely related activating innervation, kinetic and tonic, which act on a mechanism now recognized as being located largely in the spinal cord (Kraus and Rabiner [2] and Wilson [3]). This mechanism in turn determines various postures, linking cells for integration of their activity.

The relation of the postural element of motile to that of rigid states has been commented on by Hunt who stated, "Movements are followed by their attendant postures like shadows." In a moving picture camera the number of postures in successive pictures depends on the number of pictures taken in a given period of time. At ordinary speed, sixteen postures are registered per second; in bradykinetic analysis as many as 300 pictures per second may be registered. Theoretically, therefore, it is apparent that the postures possible in any given movement are infinite in number. It is also apparent that posture is as much a characteristic of motile states as of rigid states in which it is, however, more evident.

The change in the motor activities of patients is still another aspect to be considered. A patient may at one stage show active choreiform or athetoid movements of the limbs and trunk, and at a later stage his muscles may be fixed and rigid. In such cases increase of the tonic impulses gradually destroys the free movement of the motile stage and produces rigidity. Patients rigidly held by hypertonus are often said to have a paralysis of voluntary power. This, as a rule, is not true, as may be demonstrated by passively moving the fingers and toes and then asking the patient to move them. Voluntary power is prevented from action, but the corticospinal pathway is intact and potentially active. Its activity is merely concealed. Such cases should be described as rigidity in flexion, extension, etc., not as paralysis, paraplegia, etc.

Clinical observations show that the final rigid position is the maximum deviation from the position of rest that existed in the former motile state. This observation may be applied not only to cases which at two different stages of their development have shown motile and rigid states, but also, using a grouping and classification of stereotyped postures and stereotyped movements, to cases with rigidity alone, which may be shown to have a posture that corresponds to the maximum deviation from the position of rest of the corresponding motile state.

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2. Kraus, W. M., and Rabiner, A. M.: On the Production of Neuromuscular Patterns by Release of Spinal Integrations After Decerebration, J. Neurol. & Psychopath. **3**:209 (Nov.) 1922.

3. Wilson, S. A. K.: The Old Motor System and the New, Arch. Neurol. & Psychiat. **11**:385 (April) 1924.

and to cases showing only motile elements, in which it may be postulated that the later rigid state, if it develops, will also correspond to the maximum deviation from the position of rest of the corresponding stereotyped motile state.

To make this latter point clear it is necessary to classify stereotyped postures and stereotyped movements in simple groups. It is also necessary to state what factors may make it impossible for these stereotyped postures or stereotyped movements to appear.

GROUPING OF STEREOTYPED MOVEMENTS AND POSTURES

Spinal Appendicular.—The postures of group I (table 1) are those of decapitate and decerebrate states. The decerebrate preparation shows not only extension in the limbs but also flexion (Bazett and Penfield,[4] Magnus,[5] and Kraus and Rabiner[2]). The muscles that produce the "extension" phases are the antagonists of those that produce the

TABLE 1.—*Postures of Rigid and Motile States*

Group I.	Spinal appendicular	
	A. 1.	"Flexion"* of leg, DVD, third phase of gait
	2.	"Flexion"* of arm, DVD
	B. 1.	"Extension"* of leg, VDV position, fourth phase of gait. The decerebrate leg
		"Extension"* of arm, VDV. The decerebrate arm
Group II.	Spinal axial	
	1.	Opisthotonic position, D
	2.	Emprosthotonic position, V
Group III.	Supramesencephalic appendicular	
	1.	Ventral arm, VVV hemiplegia, parkinsonism, pseudobulbar palsy
	2.	Dorsal arm, DDD. Corresponding opposite
Group IV.	Combined axial and appendicular postures	
	1.	Combinations of I (A), 1 and 2, with II—2. Decerebrate postures
		I (A), 1 and 2, with II—1
	2.	Hemiplegia. Combination of I (B), 1 with III, 1
	3.	Holt phenomenon (dissolution of erectness in man)

* Quotation marks are used because, in reality, extension and flexion do not obtain at each joint. The terms are used for convenience and in deference to common usage.

"flexion" phases; these positions are, therefore, corresponding opposites. The decerebrate or "extended" arm corresponds to the "extended" leg in that the muscles producing these positions are anatomically and physiologically homologous (Kraus and Rabiner,[2] and Wilson[3]). The same applies to their opposites. Hence we have a group of two arm and two leg postures easily understood as belonging together.

These postures are determined in the spinal cord (Magnus,[5] Kraus and Rabiner[2] and Wilson[3]). The integrations concerned have been described and named.[6] The two leg postures represent the terrestrial or

4. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as Well as in the Acute Condition, Brain **45**:185 (Oct.) 1922.

5. Magnus, R.: Die Körperstellung, Berlin, Springer, 1924.

6. Kraus, W. M.: Rôle d'intégration joué par la moelle dans la determination des attitudes du tronc et des membres, Rev. neurol. **30**:289 (Oct.) 1923.

third and fourth phases of gait as described by me[7] in 1922. In that analysis of gait, it was shown that in every pace the legs show two pairs of corresponding opposite positions. The first two positions are remains of the movements of progression in aquatic animals, pendulum or finlike movements at the shoulders and hips. The legs and arms as a whole can be seen to swing backward and forward like fins. Superimposed on these first phases is the second or terrestrial pair, the third and fourth phases. These are the flexion and extension phases of leg movement described by Sherrington,[8] which remove the limb from the interfering ground (flexion or third phase) and provide support by opposing gravity and sinking to the ground (extension or fourth phase). The muscles producing the third and fourth phases are those active in the leg postures of group I.

The letters *V* and *D* in the formulas given indicate the primitive anatomic location of the muscles on the limbs, ventral or dorsal. They act at hip, knee and ankle (and toes), and shoulder, elbow and wrist (and fingers), respectively. The distribution of muscles on the dorsal and ventral aspects of the limbs and axis is given in tables 2, 3, 4 and 5.[9] The data for this classification were obtained from the following sources: Bolk,[10] Patterson,[11] Braus,[12] Schäfer and Symington,[13] and Flatau.[14]

Supramesencephalic Appendicular.—The second group of appendicular postures (group III, table 1) is simpler. It includes the familiar arm postures of classic hemiplegia, parkinsonism and pseudobulbar paralysis. That these postures are produced by identical (ventral) muscles has already been shown.[15] The corresponding opposite (produced by dorsal muscles), extension, abduction or retraction at the shoulder, and extension at elbow and wrist with moderate extension of

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7. Kraus, W. M.: The Difference Between a Muscular and a Neuromuscular Interpretation of Walking, Arch. Neurol. & Psychiat. **9**:184 (Feb.) 1923.

8. Sherrington, C. S.: Remarks on the Reflex Mechanism of the Step, Brain **33**, June, 1910.

9. Kraus, W. M.: Difference Between Muscular and Neuromuscular Interpretation of Walking, Arch. Neurol. & Psychiat. **9**:188, 191, 192 and 193 (Feb.) 1923.

10. Bolk, Louis: De segmentale Innervatie van Romp en Ledematen bij den Mensch, Haarlem, 1910.

11. Patterson, A. M., in Cunningham's Text Book of Anatomy, 1918, p. 743.

12. Braus, Hermann: Anatomie des Menschen, Berlin, Springer, 1921.

13. Shäfer and Symington, in Quain's Anatomy, "Peripheral Nerves and Sense Organs," New York, Longmans, Green & Company, 1909, p. 120.

14. Flatau, Edward: Die motorische, sensible und reflex Segmentierung im Rückenmark, M. Lewandowsky's Handbuch der Neurologie **1**:659, 1910.

15. Kraus, W. M.: An Interpretation of the Posture of Parkinsonian Syndromes in Terms of the Neuromuscular Mechanism, New York State J. Med. **22**:399 (Sept.) 1922; footnote 7.

the fingers, is beautifully illustrated in a paper by Riddoch and Buzzard [16] in a case of tetraplegia due to a gunshot wound of the cervical cord (fig. 1). In this case supraspinal impulses must have been passing to the cord since the patient could stand. It is readily seen that if the muscles antagonistic to those producing the posture in the cut were activated, the arm posture of hemiplegia would be produced.

These postures must be determined above the spinal cord and above the midbrain, since in lesions about and below the midbrain the arm posture is that of decerebration. The posture is released by lesions

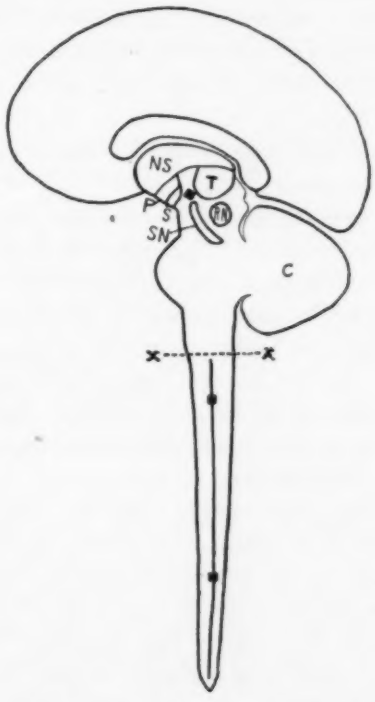

Fig. 2.—Indicating the centers of posture determination; the centers for the activation of posture by tonic and kinetic impulses are not the same. NS, neostriatum; PS, palleostriatum; T, thalamus; RN, red nucleus; SN, substantia nigra; C, cerebellum; X-X, division between the brain and spinal cord. In the spinal cord, the heavy line with two squares represents the location of the centers which determine spinal postures, so-called decerebrate postures (table 1, groups I and II); the squares indicate the special centers for arm and leg postures. The square above the midbrain represents the approximate location of the supramesencephalic arm center (table 1, group III), also the approximate location of the center of erectness in man.

16. Riddoch, George, and Buzzard, E. F.: Reflex Movements and Postural Reactions in Quadriplegia and Hemiplegia with Especial Reference to Those of the Upper Limb, Brain **44**:397 (Jan.) 1922.

causing hemiplegia, parkinsonism and pseudobulbar palsy, lesions situated in the basal ganglia. It seems most probable, therefore, that the center lies just above the midbrain (fig. 2).

Spinal Axial.—The axial group of postures (group II, table 1) is simple—a pair of corresponding opposites produced by overaction either of dorsal or of ventral axial muscles, clinically found as opisthotonos and emprosthotonos. These postures are determined in the spinal cord (fig. 2).

Combinations of Postures.—1. When the complete decerebrate state is obtained, the dorsal axial muscles produce opisthotonos (*D*), the arm is decerebrate (*VDV*) and the leg "extended" (*VDV*). As has been shown,[2] there is alternation of the muscle groups throughout: axial, dorsal; hip and shoulder, ventral; knee and elbow, dorsal; ankle, wrist, fingers and toes, ventral.

The opposite combination produced by the antagonists of the foregoing muscles also occurs.

2. The hemiplegic posture is a combination of the postures of the spinally determined "extended" leg and that of the supramesencephalically determined ventral arm. The leg posture does not correspond to that of the arm because no posture corresponding to that of the "ventral" arm (as seen in hemiplegia, parkinsonism and pseudobulbar palsy) has appeared for the human leg. The activating impulses find the prespinal, supramesencephalic arm center intact, and activate it. There is no such leg center, hence the spinal leg center is activated. Spinal man shows only flexion as a fixed leg posture (Riddoch,[17] Lhermitte [18]). It has been shown, however, that crossed extension reflexes may be obtained in spinal man, indicating that the determining centers for the postures of this movement are present in the human spinal cord. But the leg is extended, not flexed, because in man the activating center for the spinally determined leg extension is prespinal. It is uninjured by capsular and basal ganglion lesions and is then released.

3. Holt phenomenon [19] (dissolution of erectness in man): This is a combination of two reflex activities, one a forward bending of the head and trunk in bilateral disease of the basal ganglion region, the other a reflex, normally present, of flexion at the knee in response to the forward bending of the trunk. These two reflexes play an important part

17. Riddoch, George: The Reflex Functions of the Completely Divided Spinal Cord in Man, Compared with Those Associated with Less Severe Lesions, Brain **40**:264 (Nov.) 1917.

18. Lhermitte, J. J.: La section totale de la moelle, Bourges, Pardy-Pigelet et Cie, 1919.

19. Kraus, W. M.: Le phénomène de Holt. Les effets, pendant la marche, du deplacement en avant du centre de gravité du corps sur la position maxima de support de la jambe, sa signification à l'état normal et dans les conditions pathologiques, Ann. de méd. **15**:67 (Jan.) 1924.

in the postures of parkinsonism and pseudobulbar palsy. They are the reflexes which dissolve erectness.

The postures in the two diseases mentioned may also be shown to consist of hemiplegia, modified by the two reflexes described. The arm posture of the hemiplegic patient is caused by ventral muscles. The same muscles cause the arm postures of parkinsonism and pseudobulbar palsy. The legs in hemiplegia are extended, the trunk and head not bent forward, but in the other two diseases there is flexion at the knee and bending forward. As soon as the lesion becomes bilateral, the reflexes of the Holt phenomenon occur—the body bends forward, and there is secondary reflex flexion of the knees. Bilateral innervation of axial muscles and unilateral innervation of appendicular muscles is the familiar anatomic basis of these differences between unilateral and bilateral diseases.

The center for erectness in man probably lies between the basal ganglia and the midbrain regions (fig. 2).

The muscles concerned in producing all of these postures are the same as those which are active in producing movements that bring the limbs or axis into the same positions. In other words the muscles producing a given rigid posture are the same as those which produce the identical posture in the course of a movement.

FACTORS PREVENTING THE APPEARANCE OF STEREOTYPED MOVEMENTS AND POSTURES

The stereotyped postures described are common, but in many cases they are not recognizable, not precisely present. The destereotyping may be due to a number of factors:

1. Voluntary control of muscles can destroy stereotyped postures and movements. The center for this function has the essential purpose of increasing the variations of destereotyped or dissociated postures and movements; the cortex receives and stores memories of differences of sensation and activates and stores memories of differences of movement.

In flaccid states of cortical origin, stereotyped posture either is absent or becomes manifest by the activity of lower centers (contractures, associated movements).

2. There may be either a bilaterally asymmetric lesion or an incomplete lesion on one side. This applies not only to the determining centers and paths, but also to the activating centers and paths. Under these circumstances the complete stereotyped postures and movements fail to appear.

3. There may also be a lesion of the synergic system (cerebellum and connections) which prevents balanced action of antagonists.

4. There may be a lesion of entire, or parts of, peripheral neurons, motor or sensory.

If muscles cannot be activated or the proprioceptive influences from them are prevented from reaching the centers, there can be no stereotyped posture or movement. It is understood that peripheral nerve lesions produce clearly stereotyped postures, but the present discussion deals with centrally produced postures.

5. Lesions of muscles, tendons and synovial sheaths will interfere with stereotyped postures and movements.

THE RELATION OF STEREOTYPED POSTURES TO THE STEREOTYPED MOVEMENTS IN WHICH THEY MAY OCCUR

Movement either from a position of rest or in a repeated act as that of leg movement in walking may be indicated graphically. Two types of activity are to be considered, one the maximum postural deviation

Fig. 3.—*H-F*, leg in flexion; *H-A*, leg in support and extension; *H-V*, position of the leg back of the body during normal walking; *H-D*, the front of the body during normal walking. The degree of flexion of the leg so far as it applies to walking is, of course, extremely exaggerated.

occurring in a repeated stereotyped movement from the position of rest and the other the maximum postural deviation occurring in a repeated stereotyped movement as that of walking. In figure 3 both are indicated simply: (1) The withdrawal of the leg by a flexion reflex is indicated by shortening of the line *H-A* to *H-F*. The distance *H-F*, the extent of flexion, varies. (2) The production of the movement of flexion of the leg in walking as it passes from a position behind the body (*H-V*) to one in front of it (*H-D*) is indicated by the arc *V-F-D*, the maximum flexion position being *H-F*.

Movements from Positions of Rest.—The situation when the leg is withdrawn from rest (*H-A*) to flexion (*H-F*) is that *H-F* is the maximum postural deviation in the movement. The objection that the

extent to which the posture is manifested (extent of flexion at the three great joints) varies does not in the least nullify the fact that it is the maximum postural deviation from rest of this movement. The stereotyped fixed posture which may occur is produced by the same muscles that have produced the maximum postural deviation of the movement.

This applies to the postures of all stereotyped movements from a position of rest. It may be illustrated by the following case reported with photographs by Goodhart and me:[20] In a girl suffering from epidemic encephalitis and presenting the picture of dystonia musculorum, the foot, at one stage of development, moved from rest in and out of the position of cavus and inversion with toe flexion (fig. 4), "ventral foot" position of the foot produced by ventral muscles; a year later, the foot became fixed in the maximum posture of the "ventral foot" (fig. 5).

In movements of the axis producing transitorily the postures of opisthotonos and emprosthotonos the same rule obtains. The maximum postural deviation which can occur in the movement is equivalent to the maximum static posture.

Repeated Stereotyped Movements.—A similar relation exists with regard to the repeated movements of gait. When the leg goes from *H-V* through *H-F* to *H-D*, the posture *H-F* represents the maximum deviation from both *H-V* and *H-D*. Any position between *H-V* and *H-F*, or between *H-F* and *H-D*, is necessarily not the maximum of flexion. The maximum posture of the third or flexion phase of gait corresponds to that of the fixed corresponding state, flexor rigidity. The distance *F-A* may be multiplied or divided, the posture may be exaggerated or diminished, but it is always that lying midway between the minima *V* and *D*. Furthermore, the muscles producing this flexion are those concerned in the posture of the flexion reflex and of fixed flexor rigidity.

In movement one may imagine the muscles activated by intermittent stimuli which put the limb into positions farthest removed from those of rest. In rigid states the stimuli are sufficiently continuous to hold the limb in this position farthest removed from that of rest.

The rules, therefore, appear to be: (1) Every completely fixed or rigid stereotyped posture represents the maximum postural deviation assumed on deviation from rest in a corresponding stereotyped movement. The maximum postural deviation may or may not be the greatest possible deviation from that of rest. (2) A case seen during the motile state will, if and when rigidity appears, show a posture corresponding to the maximum deviation rom rest in the motile state. (3) The neuro-

20. Goodhart, S. P., and Kraus, W. M.: On Deformity of the Foot in Dystonia Musculorum, Arch. Neurol. & Psychiat. **11**:436 (April) 1924.

muscular factor which determines what the postures of a movement shall be is the same as that which determines the corresponding stereotyped static posture.

SUMMARY

The classification of postures serves to simplify this complicated problem. There is a postural element in all movements. The successive postures of a limb or the trunk during a movement are infinite in number. Hence posture is an element of both rigid and motile states.

In cases in which abnormal movements have been replaced by abnormal postures through the fixing influence of increased tonus, the final rigid position is that of the maximum possible deviation from the position of rest which existed in the motile state. This rule may be applied to all stereotyped forms of movement and posture. Recognition of this rule enables the examiner to foretell the particular posture in which a patient having a disease causing increased and increasing tonus will become fixed.

That posture determination is a separate and distinct function is thus again emphasized and the problems involved are more clearly separated from those of tonic and kinetic, i. e., activating impulses. Activation of posture by tonic or kinetic impulses is a process which always evokes the same result, muscular activity. The variations are of intensity. Determination of postures is a different process; it has not only the function of coordination, but also that of correlation of the activities of muscles. Compared with activation, it is relatively complex and involves many more neurons.

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THE RADIX SPINALIS TRIGEMINI AND THE PRINCIPLE OF USURPATION *

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One of the interesting features of the trigeminal nerve is its long caudal extension in the radix spinalis. The axons of the cells in the gasserian ganglion enter the pons and divide, one branch going to the main sensory nucleus, the other turning caudad and extending even as far as the first or second cervical segment of the spinal cord. The behavior of these fibers is far different from that of the homologous fibers in Lissauer's tract in the spinal cord. In the spinal cord these fibers run for a distance of one or at most two segments before entering the gray matter of the posterior horn whereas in the case of the spinal trigeminal tract they run for a much greater distance before terminating in the substantia gelatinosa of the bulb. The explanation for this is to be sought in the phylogenetic development of the trigeminal nerve.

The fifth nerve is not the only one that contributes fibers to the radix spinalis trigemini. The seventh, ninth and tenth cranial nerves also contribute to this root in the lower fishes, so that the similarity of the root to Lissauer's tract is quite marked. In Figure 1 which is taken from Johnston [1] the cutaneous branches of the cranial nerves are shown as they exist in the cyclostomes. In the higher fishes some of these cutaneous fibers disappear, those doing so being indicated in the illustration by broken lines. In the bony fishes the cutaneous fibers for common sensation have disappeared to a considerable extent from the seventh, ninth and tenth nerves.

These cutaneous fibers reappear in the amphibia, develop considerable importance, and then undergo regression in the reptiles. Cutaneous branches of the seventh, ninth and tenth nerves are very small, almost insignificant in birds and mammals, and only within the last twenty years have cutaneous sensory branches of these nerves in man been recognized clinically. These branches are so fine, and the areas innervated so small that until recently they practically escaped notice although the older anatomists had described cutaneous filaments for all of these lower cranial nerves.

During the development of the head, these lower branchial nerves have gradually lost their cutaneous fibers, and the trigeminal nerve has increased in importance until it has covered all of the face and a large

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* From St. Elizabeth's Hospital.

1. Johnston, J. B.: The Nervous System of Vertebrates, London, John Murray, 1907, p. 107.

part of the head. Figure 2 from Sherrington [2] via Kappers shows how the cutaneous distribution of the upper cervical roots has become diminished, and how the trigeminal nerve has usurped their fields.

Figure 3, from a previous paper by myself,[3] shows the probable extent of the sensory branches of the various cranial nerves in man, results arrived at by several different methods of investigation, anatomic dissection, residual sensibility, reflex phenomena and herpetic eruption. It can be seen that except for the region of the ear, most of which is supplied by two or three nerves, the whole of the face and head is supplied by the fifth cranial and the second cervical nerves.

Why there has been this progressive concentration of function in a single nerve is difficult to explain, except that concentration and centralization seem to be in keeping with the economy of the organism. The presence of the carotid artery in close proximity to the developing trigeminal ganglion may have influenced it favorably by according it abundant nutrition.

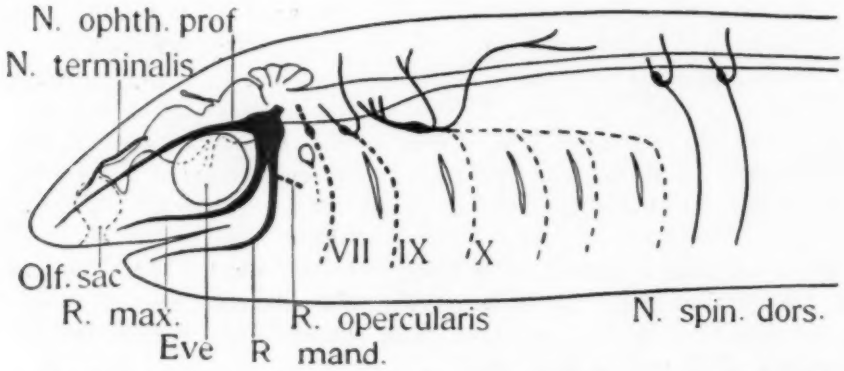

Fig. 1.—The cutaneous sensory branches of the cranial nerves in fishes. The broken lines represent branches found in cyclostomes but not yet found in other vertebrates (Johnston).

That one nerve can take over the function of another is occasionally demonstrated in man. Figure 4 *A* from Cushing [4] shows the area of anesthesia some days after extirpation of the gasserian ganglion for the relief of neuralgia. The same patient (Fig. 4 *B*) was later found to have a much smaller area of anesthesia. There had certainly been no

2. Sherrington, Charles: Experiments on Examination of the Peripheral Distribution of the Fibers of the Posterior Roots of Some of the Spinal Nerves, Part 2, Phil. Trans. Roy. Soc. London, Series B, **190**:45-186, 1898.

3. Freeman, Walter: The Columnar Arrangement of the Primary Afferent Centers in the Brain-Stem of Man, Folia neuropathol. eston. **3**:27, 1925.

4. Cushing, Harvey: The Sensory Field of the Cranial Fifth Nerve, Bull. Johns Hopkins Hosp. **15**:213, 1904.

regeneration of the fifth nerve, for Cushing states emphatically that the ganglion had been removed completely. It seems from this that the fibers from the bordering nerves had grown into the anesthetic area and connected with the sense organs already established there. Cushing states that this degree of reduction of the area of anesthesia is uncommon, yet it is none the less significant. A sensible reduction is frequently found in the months following trigeminal neurectomy. It shows conclusively that one nerve can take over an area formerly supplied by another.

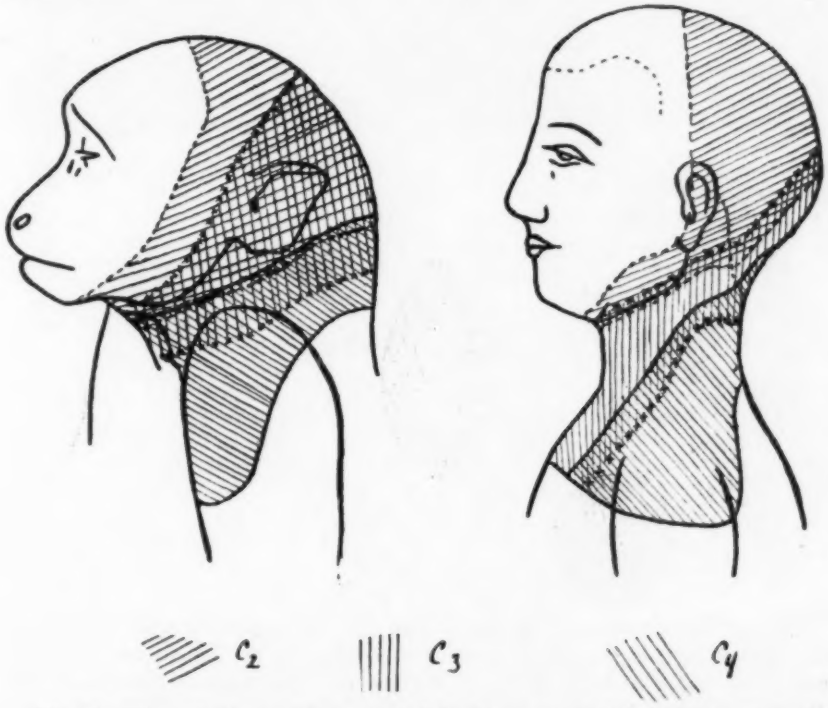

Fig. 2.—The cutaneous areas supplied by the second, third and fourth spinal nerves in the ape and in man, showing (*a*) the extent of overlap and (*b*) the reduction in importance of the cervical roots in man (Sherrington, adapted by Kappers).

If this usurpation has indeed taken place in phylogenetic development, it may then be asked why the primary receiving centers have not been collected into one place instead of extending along the greater part of the brain-stem. The main sensory nucleus of the trigeminal nerve lies at the level of entry of the nerve, so it appears rather anomalous that the descending fibers should run so far before entering into relationship with the cells of origin of the secondary pathway.

Some light is thrown on the question by a study of cases of progressive destruction of the radix spinalis, or rather of its attendant

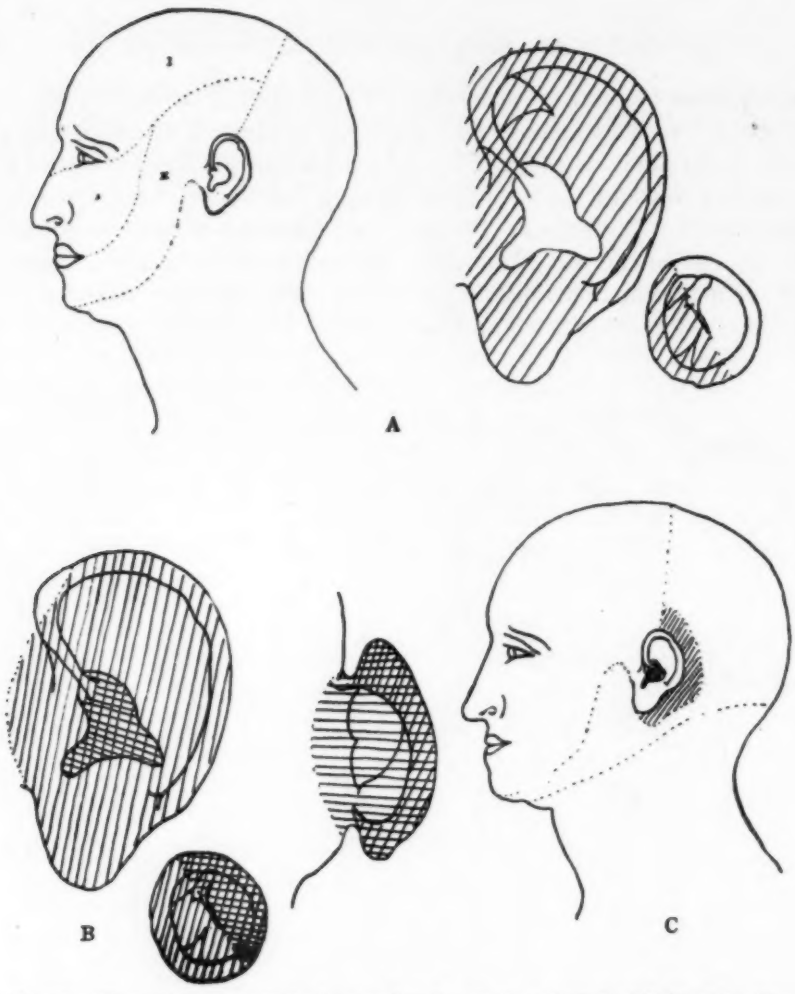

Fig. 3.—Dermatomeres of the human head. *A*, the trigeminal field: The line on the scalp and face is determined in cases of paralysis of the second and third cervical nerves as the posterior border of the sensitive area. The extension over the anterior surface of the ear is indicated by the following facts. This area is not supplied by the glossopharyngeal nerve or the vagus nerve because it is anesthetic in cases of paralysis of both fifth and seventh nerves. This area retains its cutaneous sensibility, however, after paralysis of either fifth or seventh nerve alone. *B*, the field probably supplied by the seventh and ninth nerves. The field of the seventh (vertical shading) is determined by the eruption in cases of herpes oticus. Its anterior extension in front of the tragus is found in cases of trigeminal neurectomy. The extension to the posterior surface of the helix is of unknown extent. In cases of paralysis of both fifth and seventh nerves the concha and the posterior surface of the helix are sensitive showing that they are probably innervated by the glossopharyngeal nerve (horizontal shading). The zoster zone for the glossopharyngeal nerve includes a small area in the fissure between the auricle and the mastoid region. Its posterior extent is unknown. *C*, the fields for the vagus nerve (shaded) and the second cervical segment. The intra-auricular portion is indicated by the reflex phenomena that are induced by irritation of the ear. The area surrounding the ear is the area supplied by the posterior auricular branch. The second cervical dermatomere is fairly well known through studies on residual sensibility.

Fig. 4.—*A*, the extent of anesthesia a short time after extirpation of the gasserian ganglion. The area of anesthesia is always larger than the area of analgesia. *B*, the extent of anesthesia in the same patient many months after operation. The area of anesthesia is considerably diminished by encroachment of the surrounding nerves (Cushing).

Fig. 5.—The advance of analgesia in cases of syringobulbia. As the root is progressively destroyed the sensitive area narrows until it comes to a focus about the mouth. The segmental character of the innervation about the rostral orifice is as clear as that about the anal orifice (Dejerine).

nucleus. I refer to the disease syringobulbia in which there is found in the scalp and face a syringomyelic dissociation of sensation; namely, loss of pain and temperature sensations with preservation of tactile sensibility. As the disease progresses, the zone of anesthesia narrows until it comes to a focus about the mouth (Fig. 5 from Dejerine[5]). This indicates that the substantia gelatinosa of the brain-stem is segmented in a primitive fashion, focussing on the mouth, just as the lower sacral segments of the cord focus about the anus. The mouth and the anus are the two ends of the body.

With these two facts in mind then, first that the trigeminal nerve has usurped the fields formerly supplied by several other nerves, and second that there is definite segmental representation in the spinal root of this nerve, we may arrive at an explanation of the long caudal projection of the afferent fibers. Pain, pressure, heat and cold are primitive types of sensibility accompanied by a high degree of feeling tone. They might be called paleo-esthetic sensibility. The receiving centers for these sensations are arranged in primitive fashion, segmentally, in the substantia gelatinosa rolandi in the medulla oblongata just as in the spinal cord. These centers, laid down early in the course of phylogenesis, do not change their position. Therefore, when a single nerve usurps the function of several other nerves, the fibers supplying the invaded area must travel a greater distance within the nervous axis in order to reach the cells of origin of the secondary pathway. In the case of the trigeminal nerve this probably explains the long caudal projection of the axons of cells in the gasserian ganglion.

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5. Dejerine: Sémiologie des affections du système nerveux, Paris, Masson & Cie, 1914, p. 378.

NEUROLOGIC SYMPTOMS IN OSTEITIS DEFORMANS (PAGET'S DISEASE)

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In 1876, Sir James Paget of London described a chronic bone disease now commonly called osteitis deformans, or Paget's disease. So complete was that initial description, based on the study of five cases, that clinicians have since been able to add little to the clinical knowledge of this condition. During the last few years, however, especially since 1921, when the study of bone structure was greatly facilitated by the use of the Buckey-Potter diaphragm, the diagnosis of this disease has been largely transferred from the clinician to the roentgenologist. In osteitis deformans the structure of the bone shows a picture of rarefaction and condensation with an increase in bulk and deformity that is believed to be duplicated in no other disease. Consequently, a diagnosis can be made by the roentgen rays early in the course of the disease, long before the sufferer presents the typical picture described by Paget.

The classic example of osteitis deformans is a little, old man, simian in attitude, with head disproportionately large, suggesting more a hydrocephalic condition than acromegaly, with arms hanging perhaps below the knee, with bowed and shrunken spinal column, with thickened clavicles and sunken chest, and with the long bones of the legs markedly thickened and bowed forward and outward—a figure shrunken in stature and handicapped in gait. Such a classic picture is rarely seen, but osteitis deformans, as diagnosed early in its development with the help of roentgen-ray examinations, has ceased to be a curiosity.

The incidence of the disease is shown in Table 1.

The distribution in years of the eighty cases (sixty-four since and sixteen before 1916) diagnosed at the Massachusetts General Hospital is shown in Table 2.

In this table, it will be seen that sixty-eight, or 85 per cent., of the cases have been diagnosed with the help of the roentgen rays. Only seven were recognized before 1913 when the roentgen ray was first utilized at the Massachusetts General Hospital for this purpose. Of this series of cases 91 per cent. have been diagnosed since that time. In 1917, when many of the staff were away in the war, only one case was discovered. Of the eighty cases, approximately 29 per cent. were found on the medical services, 29 per cent. on the orthopedic service, 21 per cent. on the surgical services, and only 2.5 per cent. on the neurologic service.

Dr. L. B. Morrison, a roentgenologist in Boston, who sees many orthopedic cases, has diagnosed ninety-eight cases since the beginning of 1917 among about 15,000 persons in whom the pelvis or long bones were photographed. Dr. T. R. Healy has found a dozen or more cases at a small clinic at a hospital in Newburyport, Mass. Dr. A. S. MacMillan, another roentgenologist in Boston, whose cases are often from the eye and ear or nose and throat specialists, reports having seen seventeen cases in the last three and a half years. Many of these patients had symptoms referable to the head long before the rest of the bones showed sufficient involvement to call for examination.

TABLE 1.—*Incidence of Cases*

Date	Authority	Incidence	Number of Cases
1912	Osler, Practice of Medicine	1-10,000	..
	Hurwitz at Johns Hopkins Hospital	1-10,000	3
	DeCosta at Jefferson Hospital, Philadelphia	1-12,666	3
1916	Cutler at Massachusetts General Hospital, Outpatient Department, Boston	1-40,714	7
1923	Moore at Washington University Hospital, St. Louis	1-11,000	14
1924	Newton at Peter Bent Brigham Hospital, Boston	1-2,353	17
1925	Gregg at Massachusetts General Hospital, Boston; Total Admissions, 1916-1924	1-5,114	64

TABLE 2.—*Distribution of Cases*

Date	Cases	Date	Cases
1902	2	1917	1 (all by roentgen ray)
1903	2	1918	7 (all by roentgen ray)
1905	1	1919	8 (all by roentgen ray)
1908	1	1920	7 (all by roentgen ray)
1912	1	1921	9 (all by roentgen ray)
1913	1 (1 by roentgen ray)	1922	6 (all by roentgen ray)
1914	3 (1 by roentgen ray)	1923	11 (all by roentgen ray)
1915	5 (4 by roentgen ray)	1924	8 (all by roentgen ray)
1916	7 (5 by roentgen ray)	Total	80 (68 by roentgen ray)

The symptomatology of osteitis deformans is startlingly protean, and is naturally dependent on the bone structures involved. Some investigators believe that the bones of the pelvis are first involved. At any rate, many of the patients appear in orthopedic practice because of symptoms simulating sacro-iliac disease. When the vertebrae are involved, cord symptoms may appear from compression of the cord. As previously stated, some cases show cranial symptoms long before the bones of the limbs are sufficiently altered to attract attention. When the bones of the head are involved, the neural foramina are narrowed, and symptoms referable to the cranial nerves result.

A grouping of symptoms follows: Surgical—spontaneous fractures; questions of malignant growth. Orthopedic—joint pains; periosteal pains; motor disturbances. Medical—coincidental. Neurologic—neuralgias and paralyses; cord compression; involvement of cranial nerves; facial and oculomotor paralyses; disturbances of special senses (sight, hearing, taste and smell).

REPORT OF A CASE

In the summer of 1924, a case of osteitis deformans came under my care showing a remarkable involvement of the bones of the head. A roentgenogram of the skull taken by Dr. A. S. MacMillan of Boston, who had diagnosed the condition

Appearance of skull in case of osteitis deformans.

six months previously, is shown in the accompanying figure. The patient was a married woman, aged 59, whose symptoms ran back over a period of thirty-one years when acute attacks of headache began. Neurologic examination showed involvement of six of the twelve cranial nerves, and probable involvement of four others, leaving but two of the cranial nerves intact. In spite of the discomfort from impaired sight, hearing, taste and smell, though troubled with transient attacks of facial neuralgia and an acutely sensitive scalp, lacking all the teeth which had been obtruded from the upper jaw and with obstructed nasal passages, daily vomiting attacks, painful limbs, advanced nephritis, myocardial weakness and general arteriosclerosis, this patient was reported in May, 1925, as being in about the same condition as when seen by me in the summer of 1924, although somewhat fatigued after a trip to California and back during the winter. Such is the chronicity of this disease.

CONCLUSIONS

Osteitis deformans is not rare. Long before the stage of gross deformity it gives rise to neurologic symptoms, such as pain and interference with the function of the nerves crowded by the proliferating bony structures.

Osteitis deformans should be regarded as possible until ruled out by satisfactory roentgenologic examination in cases of pathologic fracture, neuritis or neuralgia of undetermined origin, and nerve disability.

Early and definite diagnosis can be made by roentgenologic examination.

Clinical and Occasional Notes

RESPIRATORY DISTURBANCES FOLLOWING EPIDEMIC ENCEPHALITIS*

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Disturbances of respiration during the acute stage of epidemic encephalitis are common and include respiratory paralysis, tachypnea, bradypnea and various types of irregularity of rate or amplitude. They may be due to inflammatory changes in the respiratory organs, to bulbar lesions or to myoclonic contractions of respiratory muscles. Less commonly among the sequelae, or in what we now regard as the chronic stage of the disease, similar disturbances occur. These phenomena were classified by Marie[1] into (1) disturbances of respiration proper, as tachypnea (either permanent or paroxysmal with periods of apnea), and bradypnea; (2) spasmodic cough, and (3) respiratory tics. They may be associated with other disturbances, such as the pseudo-Parkinson syndrome, or may be the predominating symptom. The most striking of these disturbances are attacks of alternate polypnea and apnea, which seem to be characteristic of this disease. Such cases have been reported by Vincent and Bernard,[2] Babinski and Charpentier,[3] Chiray and LaFourcade,[4] Parker,[5] Pardee,[6] Cameron,[7] Urechia and Mihalescu,[8] Marie and Lévy,[9] Suckow,[10] Stern,[11] Turner and Critchley[12] and others.

The following cases, one of permanent tachypnea and three of polypnea with apnea, were seen at the Neurology Clinic at the University Hospital.

PERMANENT TACHYPNEA

CASE 1.—A housewife, aged 33, entered the hospital June 6, 1923, complaining of nervousness and insomnia. The family and previous histories were negative. The present trouble began in February, 1923, with pain in the back of the head and delirium for three weeks. Other initial symptoms were involuntary jerking of the arms, diplopia for six weeks and insomnia. She

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*From the Neurology Clinic of the University Hospital.

1. Marie, P.; Binet, L., and Lévy, G.: Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1075 (July 7) 1922.
2. Vincent, Clovis; and Bernard, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1111 (July 21) 1922.
3. Babinski and Charpentier: Rev. neurol., November, 1922, p. 1369.
4. Chiray, M., and LaFourcade: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:406 (March 16) 1923.
5. Parker, H. L.: Disturbances of Respiratory Rhythm in Children, Arch. Neurol. & Psychiat. **8**:630 (Dec.) 1922.
6. Pardee, I. H.: Spasmodic Forced Respiration as a Sequel of Encephalitis, J. A. M. A. **80**:178 (Jan. 20) 1923.
7. Cameron, H. C.: Proc. Roy. Soc. Med. **16**:30 (April) 1923.
8. Urechia, C. I., and Mihalescu, S.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:210 (Feb. 9) 1923.
9. Marie, P., and Lévy, G.: Rev. neurol. **38**:1233 (Oct.) 1922.
10. Suckow: Monatschr. f. Psychiat. u. Neurol. **56**:317.
11. Stern: Monatschr. a. d. ges. Geburtsh. d. Neurol. u. Psychiat., No. 30, 1922.
12. Turner, W. A., and Critchley, M.: Brain **48**:72 (March) 1925.

was said to have "breathed about seven times as fast as normal" at that time. She recovered in six weeks, except for rapid breathing and insomnia, which persisted up to the time of her admission. Examination showed the patient to be well nourished and mentally normal. The respirations were about 80 a minute, regular and shallow. She could speak only one word at a time because of the extreme shortness of breath. There was no cyanosis. The pupils were equal, reacted somewhat sluggishly to light, promptly in accommodation. Lateral deviation of the eyeballs was limited in each direction. The biceps and triceps reflexes were normal. The knee jerks and Achilles jerks were slightly exaggerated. There was a medium tremor of the hands on extension. Masking of the facies and rigidity as in the Parkinson syndrome were absent. The ocular fundi showed low grade neuroretinitis. The results of the physical examination were entirely negative. A roentgenogram of the head was suggestive of a slight increase in intracranial pressure. The spinal fluid contained one cell per cubic millimeter, a slight increase in albumin and globulin and a normal amount of reducing substance. The gold curve was 2223311000. The Wassermann reaction was negative on the blood and spinal fluid. While in the hospital the patient's respirations varied from 50 to 80 per minute and were very shallow. Various drugs were tried without much improvement, but under hyoscin the respirations became somewhat deeper and the patient was much more comfortable.

Shallow respiration or micropnea has been described as due to rigidity of the diaphragm, and Suckow[10] observed with a fluoroscope that in such cases the diaphragmatic movements were slow and narrow. Micropnea is usually associated with the pseudo-Parkinson syndrome, but the rate is not markedly accelerated. In our case there were no signs of pseudo-parkinsonism, and the rate reached as high as 80 per minute. It is believed, therefore, that such tachypnea is not merely compensatory for micropnea, but depends on an underlying disturbance of central vegetative centers, possibly in the medulla. Such a lesion, by producing a change in the metabolism of the respiratory center itself, could provoke marked changes in respiration. This has been shown by the work of Gesell[13] who demonstrated the extreme sensitiveness of the respiratory centers to changes in their own metabolism, irrespective of the blood composition.

PAROXYSMAL POLYPNEA AND APNEA

Case 2.—A girl, aged 15, entered the hospital Nov. 10, 1922, complaining of attacks of respiratory difficulty. The family history was unimportant. She had had measles, an appendectomy three years previously, and "influenza" each year from 1918 to 1922. The present illness began in February, 1920, with diplopia which lasted about a week. There was no history of fever at the time. For the first four days she was restless and complained of insomnia, following which she slept continuously for two days. Since that time there had been persistent insomnia. She had no other complaints until June, 1920, when the respiratory attacks began, and in March, 1921, the attacks necessitated her confinement at home. In the attacks, as observed, she first stood up with the body bent backward and held rigidly, taking a deep inspiration lasting about ten seconds; this was followed by a varying number of deep and rapid respirations (about 40 a minute) with the body relaxed when she again held her breath in full inspiration. This cycle would be repeated many times. Occasionally during the prolonged inspiration, she crouched to the floor, sticking

13. Gesell, R.: Am. J. Physiol. **66**:5 (Sept.) 1923.

her tongue out to one side of the mouth and making various facial grimaces. There was slight flushing of the face during the inspiratory stage. She seemed fully conscious throughout the attacks but was unable to speak. She never bit her tongue, was never incontinent, and appeared normal after attacks and not drowsy. At the time of admission the attacks were almost incessant. They were partially controllable, as in public places, but such control was attended by a distinctly uncomfortable sensation, a feeling of tension, and later she

Fig. 1.—Apneic phase of attack.

would have to be allowed to "get them out of her system." Since the onset of attacks the patient's family had noticed a change in her character—she had become rather careless and destructive.

She walked slowly but there was no masking of the facies nor tremor of the parkinsonian type. She replied promptly but appeared below par mentally. The results of the physical examination and tests of the blood and urine were entirely normal. The pupils were equal, the right reacted a little sluggishly to light. The ocular movements were normal, but there was a fine rotary nystagmus on deviation of the eyeballs in any direction. The skin and tendon

reflexes, sensation and ocular fundi were normal. During sleep and between attacks the respirations were quiet and regular.

Case 3.—A youth, aged 19, entered the hospital Nov. 30, 1922, complaining of attacks of difficult respiration. The family and personal histories were unimportant. The present illness began in November, 1920, when he was delirious and hallucinated, but could be easily aroused, and would reply normally. He developed a slight fever and became "sleepy." This lasted a few days, and then he apparently recovered, returned to school and was well until the summer of 1921, when he began to have respiratory attacks. They began as spells of difficult respiration which gradually increased in frequency and severity up to the time of admission. In the attacks he stood up with the body bent backward, and arms held outward and behind (Fig. 1) taking a deep and prolonged

Fig. 2.—Tachypneic phase of attack.

inspiration. This would last from five to ten seconds. He then leaned forward placing the hands on the knees (Fig. 2) and breathing rapidly for about ten seconds, when he again assumed the former position, holding his breath in full inspiration and emitting a peculiar laryngeal bruit. The attacks were under his control when he desired, but after controlling them for awhile he felt compelled to seek relief through them. He slept well, during which time the respirations were normal, as they were between attacks.

He was well nourished and results of physical examination were essentially negative. In walking he leaned forward slightly, the gait being slow and shuffling. There was masking of the facies but no tremor. The pupils were equal and reacted normally; ocular movements were normal. Skin and tendon reflexes and sensation were normal. The ocular fundi showed mild neuroretinitis. The blood, spinal fluid and urine were normal. Fluoroscopic examination of the diaphragm showed no disturbance of its action. No mental change or alteration of character could be noted.

CASE 4.—A youth, aged 18, entered the hospital Jan. 6, 1923, complaining of "stretching spells." The family and personal histories were negative. The present illness began in the spring of 1921 with an attack of sharp pains in all four extremities, and blurring of vision. There was no diplopia or lethargy, but rather insomnia up to the time of admittance. He was well but "lacked ambition" until December, 1922. At that time he began to have "stretching spells." At first they occurred only on arising, but they gradually increased to three or four daily and finally to one every few minutes. They were less frequent when he was lying down. In the attacks he would stand or lie stretched out with the entire body quite rigid, the trunk bowed forward and the head and arms back, holding his breath in full inspiration and emitting a peculiar groan. This would be followed by a number of rapid respirations with the body relaxed, when the former attitude would be resumed. He was fully conscious during attacks, but unable to speak. The attacks could occasionally be aborted by stimuli such as striking the abdomen. Sometimes he fell to the floor. There was no incontinence, and he never slept following an attack. The attacks were less frequent when his attention was diverted; and he said, "When my mind is occupied I don't have them." They were more frequent with emotional upsets, and were controllable at times but this was too unpleasant for him to attempt except for short periods.

He was well nourished and the results of the physical examination were negative. The pupils were normal but neither eyeball moved outward as far as it should, and there was rapid nystagmus on lateral deviation. There was no atrophy, deformity, paralysis or tremor. The skin and tendon reflexes and sensation were normal. The retina was slightly hyperemic. The blood and urine were normal. The spinal fluid showed a slightly positive Pandy reaction but was otherwise normal. The carbon dioxid tension of the blood was normal. Fluoroscopic examination showed "a suggestion of spasm on the right side of the diaphragm." During sleep the respirations were quiet and of normal rate. A brain puncture was made by a surgeon and a brain plug removed from the region of the caudate nucleus. The material obtained showed no active inflammation, no perivascular infiltration. The nerve cells appeared normal but there was slight neuroglia proliferation.

COMMENT

These latter cases present a history of mild febrile attack with signs of cephalic involvement. This was followed by apparent recovery, and then in a period ranging from four months to two years, there gradually developed attacks of respiratory difficulty. Two of the three cases were associated with pseudo-Parkinson features, as slowness of movement, masked facies and muscular rigidity. The ages ranged from 15 to 19, but similar cases are reported by Vincent and Bernard[3] from 4 to 48 years of age, and Cameron[7] reported one in an infant of 16 months. The attacks were attended by an irresistible impulse, and were partially controllable but control led to a feeling of tension within, necessitating relief in an attack. In all respirations were normal between attacks and during sleep. Therapeutically nothing was found of much value. Psychotherapy, persuasion and restraint were ineffective as were the use of hyoscine, phenobarbital, benzyl benzoate, peptone, strychnine, alcohol, atropine and copper sulphate.

The cause of these attacks is not clear. They first appeared to be hysterical. However, other signs of hysteria were not present, and psychotherapy produced only temporary results in our cases and in those reported by others. The attacks also have many of the attributes of tic. They are accompanied by an

irresistible impulse, are partially controllable, and are relieved by distraction of the attention. Peck[14] reported two cases of similar description without any history of encephalitis, which he regarded as true tic. But other post-encephalitic phenomena simulate tic, and Rosenow[15] has shown that some tics have an organic basis. He has produced similar attacks in rabbits by the injection of cultures from the teeth, tonsils and nasopharynx of patients with similar respiratory attacks.

The similarity of cases reported in all ages and in several countries supports the view that there is an underlying lesion in the central nervous system. No disturbance in the peripheral organs or in the blood composition has been found. Vincent and Bernard first explained the attacks on the basis of diaphragmatic inertia, leading to more or less contracture of the inspiratory muscles, attacks then being precipitated by any demand for increased oxygenation. We found no definite evidence of diaphragmatic inertia in our cases.

In the presence of rather diffuse lesions in the brain, it is difficult to localize the pathologic change responsible for this syndrome. The presence of pseudo-Parkinson features, sleep disturbance and emotional instability suggest a lesion of the basal ganglia. This is the site of predilection for the virus of this disease. Little is known of the existence of a respiratory center here, although D'Onghia[16] believes there is a center for the control of the synergy and rhythm of respiration in the thalamus, this center acting especially during laughter and weeping.

It is well known that the respiratory functions are closely related to emotional phenomena. De Massary and Walser[17] describe respiratory attacks occurring as the result of anxiety on the basis of constitutional hyperemotivity in which there is a sensation of thoracic oppression, with inspiratory spasms. In the encephalitic cases there is marked emotional instability, a tendency to exaggerated emotional response. The attacks seem precipitated by emotional stimuli arising from external factors or from within the patient's own psyche. They simulate the familiar attacks of forced laughing and crying, indicating a diminished cortical control of emotional phenomena. The lesion producing such conditions is believed to be located in central projection paths, most probably in the region of the thalamus.

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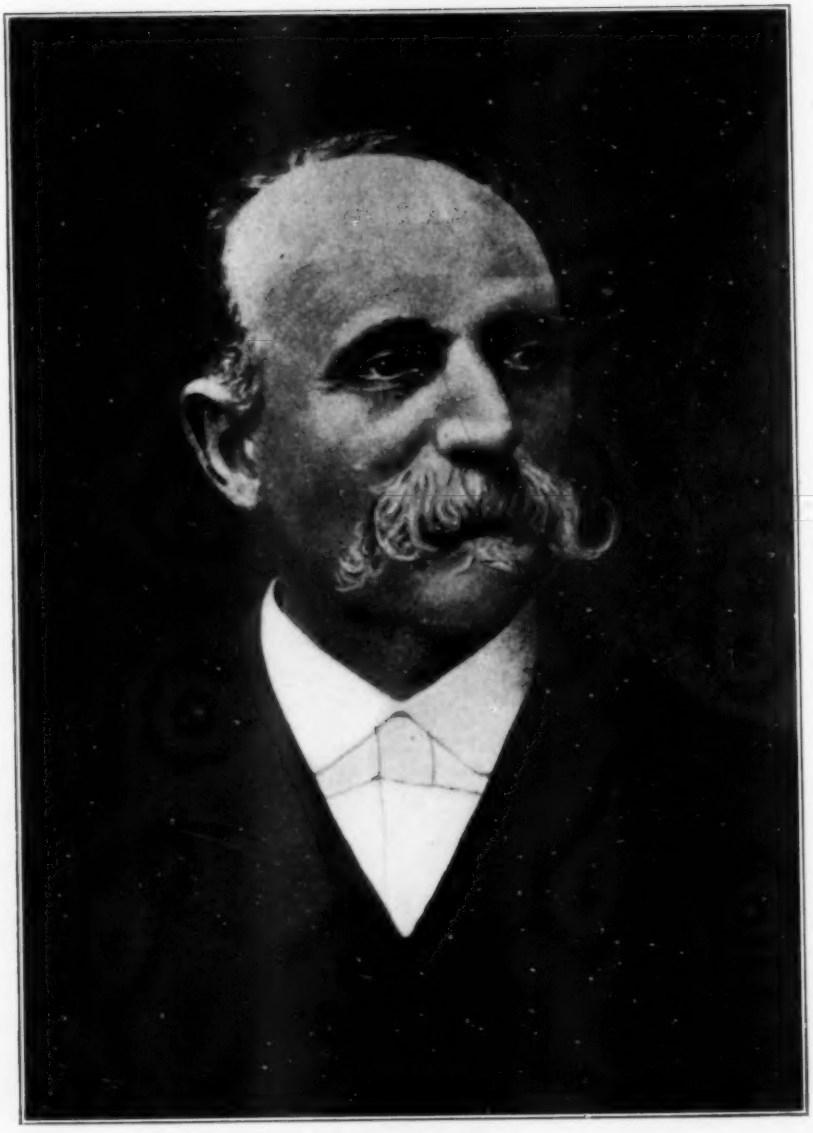
14. Peck: J. Nerv. & Ment. Dis., October, 1923, p. 297.
15. Rosenow, E. C.: J. Nerv. & Ment. Dis., January, 1924, p. 1; ibid., February, 1924, p. 155; J. Infect. Dis. **32**:41 (Jan.) 1923.
16. D'Onghia: Riforma med. **37**:1193 (Dec. 17) 1924.
17. De Massary, E., and Walser, J.: Bull. Acad. de méd. **89**:33 (Jan. 2) 1923.



CAMILLO GOLGI

(Courtesy of the Journal of Comparative Neurology.)

Obituary

CAMILLO GOLGI, 1843-1926

Prof. Camillo Golgi, renowned for his investigation of the minute architecture of the central nervous system, died in Italy, Jan. 21, 1926, in his eighty-third year.

He was born July 7, 1843, at Corteno, a small Lombardy town near Bresciano, where his father was a practitioner. He studied under Lombroso and other distinguished teachers at Pavia. After graduating from the university, in 1865, he went to the small village of Abbiategrasso, a few miles north of Milan, where he began general practice and also assumed the duties of chief resident physician in the Home for Incurables. It was in the small laboratory of this hospital, far from the great centers of scientific activity, that Golgi did his first work on the pathology and the anatomy of the central nervous system, and worked out his epoch-making staining method, *dell'impregnazione nera o cromo-argentea,* which enabled him to see the nerve cells and their finest ramifications stained black against a yellow background. Although the importance of the latter research was not fully appreciated at the time Golgi was in Abbiategrasso, his careful studies in pathology were soon noticed by his old teachers, and in 1875, ten years after his graduation, he was called to the chair of histology in his own university. Until he retired in 1918 from active teaching, he occupied a position on the faculty at Pavia, as a teacher of either histology or pathology for forty-three years, except for very brief intervals at Siena and Turin. As late as January, 1924, Da Fano visited him and reported that "he had preserved the astonishing lucidity of his marvellous mind and was taking an active part in the public life of his country and scientific activities of the University of Pavia" (*Nature* **117**: 203, 1926).

His published works fall into three natural groups: first, his studies on the minute structure of the central nervous system, after his discovery and perfection of a staining method for nerve cells and their processes; secondly, his work on the plasmodium of malaria and its relation to the clinical aspects of the disease, and, thirdly, his other papers on a variety of subjects. We will first consider his work on neuro-anatomy, which began early in his life, in the Abbiategrasso period, and lasted throughout his scientific career.

The first hint of a new staining method appeared in a paper on "The Gray Substance of the Brain" (*Gazz. med. ital. lomb.* **6**: 244, 1873), although two papers on the anatomy of the brain were issued from the same laboratory in 1870 and 1871. Apparently Golgi, not satisfied

with the usual staining methods, tried various solutions until the chromate of silver method was evolved. By this method, by no means easy to use, Golgi was able to show the finest ramifications of the protoplasmic processes of cells. After two more years of work he published a paper on the cells in the olfactory bulb and showed the first pictures of nerve cells stained by his new method (*Riv. Sper. di freniat.*, 1875). A new and profitable field of investigation had been opened by an improvement in the staining method used to visualize nerve tissue. The same year Golgi moved to Pavia as professor of histology.

The growth of our knowledge of the anatomy of the nervous system has run hand in hand, as Van Gehuchten has pointed out (Anatomie du Système Nerveux, Ed. 3, Louvain, 1900), with the development of our operative technic. In the early nineteenth century Reil was able to describe the external appearance of the brain and its fissures. With the advent of better preserving methods, Ehrenberg in 1833 was able to make out some of the nerve pathways and von Helmholtz, Remak and Purkinje (1838-1840), with crude cutting methods, described the larger cells. Stilling, first to cut serial sections, opened up a still wider field, so that he, working with Meynert, made more discoveries than all the workers before them. The change from alcohol to chromic acid and potassium bichromate, giving increased consistency to the tissue, opened the way for still further investigation. Wagner (1851) and Deiters (1864) first showed that each nerve process takes its origin in a single cell, an observation which led to the secondary degeneration studies of Türck, Bouchard, Charcot, Flechsig and von Monakow, the experimental methods of Singer and Marchi, Gudden's atrophy and the embryologic work of Flechsig and His. All these discoveries were greatly enhanced by the introduction of staining methods, first by Gerlach (1858) and later by Weigert (1884), Marchi and many others. Golgi's work, first noted in 1873, made possible a more detailed study of the minute architecture of the nerve cells and their processes. His papers on this subject, with descriptions of his staining methods, were collected and published in a folio volume, illustrated with superb drawings by Golgi, in 1886 (Sulla fina anatomia degli organi centrali del sistema nervoso, Milano, 1886) and in German in 1894 (Untersuchungen über den feineren Bau des centralen and peripherischen Nervensystems, Jena, Gustav Fischer, 1894). Much of this work appeared in parts in the *Rivista sperimentale di freniatria* (1882-1885), a journal of which Golgi became coeditor in 1882. Golgi also edited and wrote in large part, with Tenchini, a two volume anatomy (Sistema Nerverso Centrale, Milano, 1883-1889).

Golgi's method led to his description of two main types of cells, type I and type II. The cells of type I are characterized by a much

branched protoplasmic process and a single axis-cylinder process, which, as Golgi was the first to show, may have side branches also. In cells of type II, the axon is even more branched, forming a fine network in a dendritic manner. He also showed that the protoplasmic processes branched manifoldly without anastomosing, all running out ultimately to terminate blindly. Unfortunately Golgi was not content with his objective examinations. He made hypotheses in regard to the function of cells and their processes, stating that the type I cells were motor and the type II sensory. The dendrites, he thought, were not part of the conducting mechanism but were for nutritional purposes. Axons were connetced in a network, an interlacement, but not an actual anastomosis (*Arch. ital. de biol.* **15**, 1891). The work of Forel and His, aided by the studies of Nansen, cleared away this erroneous belief and stopped the discussion that had arisen about the relation of Golgi's work to Waldeyer's neuron theory. Cajal, working with the Golgi method, finally produced sufficient evidence to prove the "law of conduction" or "of dynamic polarization" within the neuron, a law which has received ample confirmation in later years by other workers, with the possible exception of the axons in the spinal ganglia.

Golgi's name is associated with three definite structures in the nervous system: (1) the Golgi network or intracellular reticulum (*Arch. ital. de biol.* **30,** 1898, and **31,** 1899), more recently commented on by Penfield (Brain **43:** 290, 1920); (2) the organs of Golgi in the tendons (1880), and (3) the Golgi cells in the cerebellum. In addition, one frequently finds references to the Golgi cells, types I and II.

His second contribution to science is his work on malaria. As Barker points out "his fame as an investigator does not depend entirely on his brilliant researches on the nervous system. His studies of the different varieties of malarial parasites transformed clinical ideas on the subject and would alone have sufficed to make his name lasting" (The Nervous System, New York, 1899). In 1885, five years after Laveran had discovered the parasites in the blood and the same year that Marchiafava gave the name *Plasmodium malariae* to the organisms, Golgi proved that quartan malarial fever depended on a specific form of the plasmodium (*Arch. per le sc. med.,* 1886). We also owe to him the discovery that the malarial paroxysm always coincides with the segmentation or sporulation of a group of parasites. Occurring every forty-eight hours the segmentation causes a tertian fever, while if it occurs every seventy-two hours, a quartan fever (*Gazz. d. osp.,* 1886). In 1886 he was first to describe the tertiary plasmodium. He described the quotidian fever and said that it might be due to double infection with the tertian plasmodium, each group sporulating on successive days. These observations were soon confirmed by other workers. Additional

contributions were made to our knowledge of the plasmodium in 1889 (*Arch. per le sc. med.* 13: 173, 1889). The first photographs of the organism appeared the next year (*Ztschr. f. Hyg.*, 1890). The estivo-autumnal type of malaria was described as a separate entity in 1893 (*Gazz. med. di Pavia*, 1893).

Golgi's writings on other subjects were numerous and important. His first paper, on "Pellagra," describes a single case with careful necropsy, apparently from his service at the Home for Incurables, Abbiategrasso (*Gazz. med. ital. lomb.*, 1868). His old master, Lombroso, who gave twenty-five years of his life to work on this disease which was very prevalent in Lombardy, stimulated him to study it. The next year a long analysis of the symptomatology and etiology of cases of mental disease appeared (*Ann. univ. di med.*, 1869). Two papers followed of more than usual interest from such a young man, on "Psammoma" and "The Lymphatics of the Brain." Work on gliomas appeared in 1875, and four papers on "Transfusion" between 1879 and 1880. Other papers are: "Normal and Pathological Voluntary Muscle" (*Arch. per le sc. med.*, 1880), "Uriniferous Tubules" (*Rendic. d. Roy. Accad. dei Lincei*, 1889) with a superb plate, "Peptic Glands in Mammals" (*Arch. ital. de biol.*, 1893) and "Rabies" (*Berl. klin. Wchnschr.*, 1894). His interest in rabies continued and it was in his laboratory that Negri first demonstrated the cell bodies now known as "Negri bodies." Since 1900, Golgi's work had been almost entirely on the finer anatomy of the neurofibrils and the internal apparatus of the nerve cells.

His collected works have appeared in three handsome volumes, the first two on histology (1870-1902) and the last on pathology (1868-1894)—(Golgi, Camillo: Opera Omnia, 3 vol., Milano, Ulrico Hoepli, 1903). Only 325 copies were issued.

Golgi was a member of many medical societies and received unusual honors and prizes. He held membership in the following societies: Accademia dei Lincei di Rome, Istituto Lombardo, Società italiana delle Scienze, the American Neurological Association, and societies of medicine or allied branches in Berlin, Petrograd, Vienna and Paris. He received an honorary Doctor of Science degree from Cambridge University. As late as Jan. 19, 1926, a few days before he died, he was made an honorary fellow of the Royal Society of Medicine, London. Some of his prizes were as follows: the Premio Riberi of the Academy of Medicine, Turin, in 1893; the Premio Fossati of the Lombardy Institute in 1880; the Reinecker prize of Würzburg, in 1894, and, jointly with Cajal of Madrid, the Nobel prize in 1906. In 1894 he received a grant from the Thompson Fund, Boston.

Golgi's position in the annals of medicine is thus assured. He made great contributions to our knowledge of neurohistology and stimulated

in others further research along similar lines. His writings on the subject of malaria were not less important. When he retired from active teaching in 1918, the *Journal of Comparative Neurology,* in its dedicatory volume, spoke of him as follows: "Camillo Golgi, savant and citizen, guardian of public health and student of histology, to whom the world is indebted for a method which gave a deeper insight into the architecture of the central nervous system." He brought honor to his profession, and by his death medical science loses one of the outstanding figures of the latter half of the nineteenth century.

HENRY R. VIETS, Boston.

News and Comment

FIFTY-SECOND ANNUAL MEETING OF THE AMERICAN NEUROLOGICAL ASSOCIATION

The next meeting of the American Neurological Association will be held in Atlantic City, June 1, 2 and 3, 1926, in the Hotel Ambassador.

THE NATIONAL ASSOCIATION FOR THE STUDY OF EPILEPSY

The next meeting of the National Association for the Study of Epilepsy will be held in New York in the Hotel Waldorf Astoria, June 7, 1926.

THE AMERICAN PSYCHIATRIC ASSOCIATION

The American Psychiatric Association will hold its next annual meeting in New York in the Hotel Waldorf Astoria, June 8 to 11, 1926, inclusive.

Abstracts from Current Literature

MEINE ERFAHRUNGEN UEBER DIE MALARIA BEHANDLUNG DER PARALYSE. M. NONNE, Med. Klin. **21**:1829 (Dec. 4) 1925.

Nonne has treated 450 paretic and thirty tabetic patients with malaria injections, with 30 per cent efficiency. These results correspond with those reported by a large number of neurologists, which Nonne quotes in detail. It may be assumed, then, that 30 per cent of these patients were cured, in the sense that: (1) their mental condition was practically normal and they were capable of following their regular occupations; (2) they were capable of doing work of a less strenuous character; (3) they were no longer in need of institutional care, but not capable of doing their regular work; (4) their condition was unchanged. Of those that were cured, quite a number obtained better positions and higher callings than they had before. A number of illustrations are given. Nonne is one of the older neurologists and says that he has treated many paretic patients and remissions such as he is reporting were not seen before this treatment was used. Not only cases that set in with excitement but also cases starting out with mild dementia have a favorable prognosis. Chronic cases of longer duration have not a happy outlook, as so far the author has seen no such cases successfully treated. The earlier a case comes under treatment, the more readily does it respond.

It is fortunate that now, with our diagnostic methods, paresis is more readily recognized than formerly. As an illustration the author mentions a patient who came to him because of disturbance of sleep and loss of energy. The only objective finding was irregularity of pupils and a sluggish response to light. However, the spinal fluid examination made possible the diagnosis of paresis. Such cases are not uncommon and the clinical teacher cannot too strongly emphasize their importance to his students. The question arises whether such cases should be given the malaria treatment, since there are stationary types of paresis as well as of tabes. However, these are the exception and the author believes that one is taking a chance in not treating these cases promptly. Of course, the responsibility of the physician is grave.

The death rate, which is also a fairly accurate guide in the malaria treatment, is from 8 to 12 per cent. In the author's cases he had twenty-six deaths (8 per cent) during or pursuant to the malaria treatment. The cause of death in thirteen cases was debility and exhaustion. The remaining deaths were due to bronchopneumonia, pneumonia, embolism, sepsis and paralytic ileus. Four deaths were in persons who had lived in the tropics, and this corroborates the observations of Mühlens and Kirschbaum that the greatest danger in administering the malaria treatment is in tropical cases. Nonne, as does Mühlens, cautions the practitioner as follows: (1) a paretic patient inoculated with malaria is to be looked on as a patient who is seriously ill and is to be treated only in a hospital or clinic where experienced physicians are always at hand; (2) the treatment should not be administered to people who react poorly or who have poor resistance; (3) only pure tertian malaria should be used, and it should have made a number of passages; (4) the blood should be controlled every day so that the treatment may be discontinued if there is an overflow of malaria into the blood; (5) patients should be dismissed only after they have been free from parasites for three weeks. Only in a few cases was the spleen

palpable. It is as yet unknown why the classic malaria does not cause a swelling of the spleen. The author has never observed a ruptured spleen, nor has he found women any more susceptible than men.

It is interesting to note that the same strain of malaria does not by any means always bring about the same form of fever. A chart is shown giving various temperature curves. In two of the author's cases there has been no reaction on repeated inoculations, and in a number of instances the chill and fever phenomena ceased spontaneously and could not be called forth again by renewed inoculations. These are cases exhibiting individual immunity.

In some cases definite psychic improvement was noted during the fever period. In most cases, however, the improvement did not take place for from several days to several weeks after the treatment was started. In one case no improvement was noted for six months. One patient was dismissed whose condition had become much worse, with the fluid highly positive. He appeared again in two years, had not been treated in the meantime and since one year had been well; no psychic defects were found and the fluid was absolutely negative. In a few cases the mental condition grew markedly worse, partly during the treatment and partly after. One patient developed a definite catatonic picture during the treatment and in six weeks was intellectually normal. One patient after treatment became asocial and was so bad that he could not be allowed in the ward. Observation during the following two months showed no improvement. Also some cases developed severe excitement during the fever period, but this soon subsided.

Mühlens advises discontinuance of treatment if the plasmodia in the blood are numerous, and therefore advises daily examination of the blood for plasmodia. Nonne has seen collapse when the plasmodia did not exceed the usual count, and on the other hand, has seen patients with many plasmodia who have withstood the attack very well.

Wagner von Jauregg has recently advised the following method for patients with lowered vitality: (1) administration of the treatment in two sessions that are separated by an interval of several weeks; (2) alleviation of fever by not more than 0.25 Gm. of quinine; (3) intracutaneous inoculation, by which the quotidian type is frequently avoided.

Skolweit has examined the blood of paretic patients before and after the fever period. It is well known that lymphocytes play a material rôle in syphilis and other infectious diseases. In the usual late syphilis, Skolweit has found in the cerebral type lymphocytosis; in paresis lymphopenia. He also has found that at the end of the attack there immediately occurred a strong lymphocytosis in the blood, which continued for a long time, then gradually diminished, and that in paretic patients with a remission, the lymphocyte value was similar to that in cerebral syphilis. He, therefore, received the impression that through intercurrent malarial injections the relation between virus and organism received impetus so that the paretic patient reacts more like a late syphilitic patient. Further investigation along this line would be highly desirable.

A much discussed question is whether the malaria treatment should be given in connection with other specific treatment. Nonne has tried all methods and has found no noticeable difference in any of them; he has seen the same good results with malaria in which no other treatment followed. Whether the malaria treatment should be repeated depends on the case. If the condition threatens to become worse a repetition is advisable.

The author's studies in 1924 have confirmed the fact that the spinal fluid findings are not always consistent with the usual clinical picture, and he repeats that positive or negative fluids may be present in a clinical cure, and that clinical deterioration may be accompanied by positive or negative fluid.

Two sections are reproduced from cases in which death followed malaria treatment, one showing an inflammatory process of the pia and vessels with no apparent change in cells, and the second showing diffuse insular areas of cell infiltrations in which inflammatory processes have entirely disappeared.

The author has treated thirty-six cases of tabes with malaria injections and says that some patients grew definitely better, but the improvement was no greater than had been obtained by other clinical methods of treatment. In more cases the irritation symptoms recurred after many weeks of remission. Also, a number of tabetic patients have withstood the cure in spite of pronounced aortitis. The author has observed that in many cases lancinating pains and gastric crises increased during the fever or recurred, or occurred for the first time. These symptoms continued only while the fever was present.

From Nonne's material he has concluded that the fever treatment in paresis (according to Wagner von Jauregg) is preferable to any other method; he has not yet been convinced of the same for tabes.

MOERSCH, Rochester, Minn.

THE STRIATAL SYMPTOM-COMPLEX IN GENERAL PARALYSIS. H. STECK, Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:424 (July) 1925.

In the extensive literature on the striatal symptom-complex which has appeared in recent years, cases of general paralysis have been reported at times with symptoms which point to an involvement of the corpus striatum. Cases described by C. Liepmann and O. Vogt, Fischer, Forester, Jakob, Boas, et al. demonstrated outspoken striatal symptoms, either true parkinsonism or choreo-athetosic disturbances. These cases, however, were relatively rare. At present we are in a position to investigate this question more carefully, since the researches of Alzheimer, Spatz, Spielmeyer, Jakob and Kolnin, all of whom showed that changes are found in the caudate nucleus and putamen regularly, whereas the globus pallidus is practically free of pathologic change. The author studied twenty-five general paralytic brains with special reference to glia formation, by the method of Cajal, and was able to confirm these investigations. He showed that not only were the caudate and putamen seats of predilection for glia proliferation in general paralysis, but also the island of Reil and the claustrum.

As Spielmeyer pointed out, an increase in the protoplasmic glia occurs in the striatum in these cases. The glia cells are increased and enlarged with long projecting processes, but with no syncytial formation. Their growth is in close relation to the blood vessels around which as a center they seem to proliferate and toward which their processes seem to reach out. Such glia proliferation is characteristic of the nuclear substance of the striatum and the cortex, whereas in the globus pallidus, thalamus and neostriatum, the glia is of a finer, spindle-like formation with thick bundles of fine fibrils reaching out for short distances. The most marked glia proliferation is found in the striatum around the lacunae caused by changes in the vessels, leading very often in general paralysis to a status cribratus. Such a state is not unlike the pathologic picture in arteriosclerosis with rigidity, but the characteristic picture in general paralysis is the diffuse glia proliferation throughout the neostriatum

in conjunction with an increase in the blood vessels. The latter differentiates the process from Huntington's chorea. The globus pallidus and thalamus are affected as described. The observation of Spatz on the increase in Hortega cells and rod cells was confirmed by the author in several cases. He found also similar findings in the cornu ammonis, island of Reil and claustrum. Nissl preparations in the majority of the cases showed little or no perivascular infiltration. In a few cases, however, definite plasma cell infiltration was present in the pallidum, the substantia nigra and the gray matter of the pons. Cell changes were most marked in the striatum; while in the pallidum and thalamus the large cells were intact, in the striatum they were markedly diseased. Many of the cells had no nuclei, Nissl bodies were few, and there was a good deal of fat in the protoplasm. This last state was most marked in a fatal case of general paralysis during malarial treatment. Neuronophagia was very common around large and small nerve cells. No exact parallel could be established, however, between the changes in the striatum and the clinical symptoms.

It is surprising that with such marked changes in the striatum, one does not find striatal symptoms more frequently. This can be explained physiologically to a certain degree, for Horsley found that ablation of the rolandic cortex temporarily obviates an athetosis. Reichardt believes that the terminal clinical signs of general paralysis, anomalies of body weight and metabolism and vasomotor disturbances are really manifestations of brain stem involvement. Hence it is not "cortical lesions which kill general paralytic patients, but lesions of the brain stem, among which those in the striatum belong." Steck remarks on the similarity of epidemic encephalitis and general paralysis in this regard. The most blatant examples of striatal involvement are found in the terminal cases with marked dementia. Among these cases are many which simulate remarkably closely arteriosclerosis with muscular rigidity; in one case mentioned by the author a case of arteriosclerosis was diagnosed general paralysis and necropsy revealed status cribratus of the striatum and an arteriosclerotic cortex. No general paralytic changes were noted, and the serology in the blood and fluid was negative. In fact, it was the striking similarity of the two pictures which led to this investigation.

The author describes a case of general paralysis with many striatal signs, with catatonia and with vegetative symptoms: variation in weight, seborrhea, etc. Catatonia, he remarks, is more frequent in general paralysis than seems apparent, though of course it is not common. Kraepelin remarked that it could occur in this disease. Steck cites a case of an agitated general paralytic patient, ill for four months, an acute case, which showed catatonia and negativism, and in which necropsy revealed marked glial changes in the striatum. Another case, of five months' duration, with negativism, catalepsy and stereotypy showed changes in the pons. In nineteen cases of catatonic general paralytic patients, a striatal syndrome was found in fourteen, contrary to the findings of Jakob. According to the views of Steck "the striatal symptom-complex represents organic soil for the development of the motor portion of the catatonic syndrome." Häfner, in an investigation of catatonia in general paralysis, found the hyperkinetic symptoms occurring as terminal conditions, while the akinetic manifestations occurred early. He divorces the catatonic symptoms from any cerebral pathologic change. Schröder studied catatonic states in seven cases in 1916, but did not study the basal ganglia. The author stresses the relation of catatonia to striatal disease.

ALPERS, Philadelphia.

DER WERT DER REFLEXE FÜR DIE DIAGNOSE. R. HENNEBERG, Med. Klin. **31**:1409 (Sept. 19) 1925.

Henneberg compares the nervous system to a complicated reflex apparatus with which may be included a psychic picture. As a rule, it is better to exclude psychic factors. If this is done, there are really few important reflexes, though it seems the ambition of many neurologists to have a reflex bear their name.

Twenty or thirty years ago it was not uncommon for patients with a paraplegia to be kept under observation for long periods for fear an hysteria was being dealt with. Today the knowledge of reflexes would settle such a problem in a moment. We know now that the absence of the pupillary response to light and the inability to obtain knee and ankle jerks invariably means syphilis. In a young adult the absence of abdominal reflexes and the presence of a Babinski sign usually mean multiple sclerosis, and so far as we now know there would be no other means of making such a diagnosis at such an early time. A tap with the percussion hammer on the lips and the prompt response not infrequently make the differential diagnosis between schizophrenia and epidemic encephalitis.

Probably the knee jerk is the most popular reflex. Westphal, in 1875, had his attention called to this reflex by a hypochondriac. When the knee jerk is difficult to obtain, the method of Jendrassik for reinforcement may be employed. The Achilles reflexes should be tested when the knee jerks are tested. If they cannot be obtained, reinforcement by kneeling on a chair may help. The Achilles reflex when absent is more suggestive of a peripheral lesion than absent patellar reflexes. In sciatic neuritis the absence of the ankle jerk is very helpful. Occasionally in severe sciatica the reflex is retained. Such a finding is always disconcerting and should arouse suspicions.

Increased reflexes may be present in highstrung nervous persons. If the increase is unilateral, careful search should be made for organic trouble. The same holds true for decrease in the response. As a rule, an ankle clonus indicates an organic lesion. At times a pseudoclonus is present in functional conditions. But such a clonus is usually not of as long duration and is not accompanied by other pathologic signs.

The absence of knee jerks and ankle jerks usually means syphilis or a peripheral neuritis. The neuritic process may have been so mild as to have passed unnoticed as is often true in diabetic patients. Careful examination should differentiate the question of the type of lesion. In cachectic conditions the reflexes may be diminished or even absent. This is probably due to a neuritic process or to cord changes.

Lesions of the lumbosacral region of the cord produce a diminution or loss of reflexes. (This is to be questioned.) Occasionally the deep reflexes disappear in cerebral tumor and hydrocephalus. The author states that in such cases a degeneration of the lumbar roots occurs as a result of pressure or toxicity. Severe acute lesions of the brain or cord are accompanied by diminution or loss of reflexes. Most authors believe this to be due to shock. In partial or total transverse lesions of the cervical or dorsal cord loss of reflexes is noted. This loss of reflexes is not readily explained, and there is little doubt that at times in such lesions the reflexes are retained.

It has been stated that in hysteria the deep reflexes may be absent. This is doubted by the writer, and no such cases have come to his attention.

The increase of the leg reflexes should be looked on as a sign of pyramidal tract irritation only when a positive Babinski sign is present. The Babinski

reflex does not indicate the site of the lesion, but usually the more severe the lesion the more active the reflex.

It is the author's experience that the absence of a plantar reflex associated with diminution of the corneal and pharyngeal reflex is very suggestive of hysteria.

According to Henneberg, the Oppenheim, and Mendel-Bechterew and malleolus reflexes are less constant than the Babinski sign. The Rossolimo sign, however, is said to be more frequently positive.

The upper arm reflexes are of less importance than the leg reflexes. Differences in the reflexes on the two sides are probably the most important. The reflexes of Mayer and of Lerische are described and discussed, but no great dependence can be put on them. (The writer makes no mention of what may be considered a pyramidal tract sign in the upper extremity described by Hoffmann). Cutaneous and superficial reflexes are much more under the control of the cortex than are the deep reflexes. Absent abdominal reflexes in young people should always be investigated carefully. The superficial reflexes are also of value in the localization of spinal cord lesions.

In discussing the pupillary reflexes Henneberg takes up the various methods of testing the reactions to light and in accommodation. He calls attention to the need of testing the corneal reflex when the eye reflexes are obtained. An absent corneal reflex may be the first evidence of a fifth nerve disturbance, especially in acoustic lesions. The mouth reflexes, as the lip and the hard palate reflex, frequently aid in the differential diagnosis between an organic and a functional condition. In conclusion the writer states that a diagnosis must not be made on the absence or presence of any one reflex, but that the history and other findings must be taken into consideration.

MOERSCH, Rochester, Minn.

CHANGES IN THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL POISONING WITH ACID. LEO HESS and EUGEN POLLAK, Arb. a. d. neurol. Inst. Wien. Univers. **27**:83 (May) 1925.

The authors injected hydrochloric acid into rabbits through a stomach tube (Walther's method) in such proportions that each rabbit received within twenty-four hours 1 Gm. of normal hydrochloric acid per one kilogram of body weight; three injections were given to each animal, one third of the quantity being given at each injection. The animals became exhausted and weak, lay motionless in their cages, refused food, and usually died after the third injection.

Necropsy showed the central nervous system to be macroscopically normal. Histologic examination revealed marked changes in the anterior horn cells of the spinal cord. The ganglion cells were swollen; the tigroid substance was reduced to coarse clumps, but more often to homogeneous masses. The nuclei in many of the cells were swollen and showed a diminished amount of chromatin. Many of the cells consisted of a granular deposit, the granules varying in size, and could perhaps be regarded as allied to an incrustation of the Golgi network (Spielmeyer).

The medulla oblongata showed changes that could readily be recognized on mere inspection of the sections. The cells in the reticular substance and in the dorsal nucleus of the vagus showed much more severe changes than in the lateral nucleus or in the inferior olive, the latter appearing normal. The hypoglossal nucleus showed at its lower level only moderate cellular changes, similar to those in the anterior horn cells. The pathologic process

in the medulla affected the large and small ganglion cells to the same extent. This region also showed glial proliferation, and here and there, a glial cell showed changes that could be regarded as regressive in nature. In the substantia reticularis diseased cells were found interspersed between normal cells. The changes in the nucleus ambiguus were less marked. Above the vagus nucleus the medulla was comparatively little involved. The nuclei of the vestibular and facial nerves were practically normal. The ganglion cells in the locus ceruleus showed changes similar to those in the substantia reticularis, with slight evidence of reaction on the part of the vessels. The reactive processes in the neuroglia, however, were much more intense in this area.

The midbrain also showed histologic evidences of a toxic degeneration. The ganglion cells of the trochlearis and oculomotorius nuclei were slightly swollen, whereas the red nucleus was intact. Cellular changes were also observed in the substantia nigra, but without definite evidence of neuronophagia.

While the hypothalamic region and the gray substance around the third ventricle showed some ganglion cell changes, most of the cells were well preserved, but here and there one could see some slight glial proliferation. The cells of the corpus Luysii were intact. Except for slight diffuse ganglion cell changes, the optic thalamus was normal.

The globus pallidus showed considerable increase in the glial cells in the vicinity of the ganglion cells but no neuronophagia. In one of the animals there was found in the pallidum near the internal capsule a patch of necrosis with softening and definite involvement of the ganglion cells near the focus of softening, with a swelling of the endothelium of the vessels. The lymph spaces surrounding these vessels contained considerable débris. There was a marked reactive glial hyperplasia near the vessels.

The cortex showed cellular changes similar to those in the basal ganglia, but more cells were affected; occasionally reactive proliferating processes were also seen near the vessels. The pathologic process, however, was diffuse and not focal.

Except for some slight alterations in a few of the Purkinje cells, the cerebellum was normal.

The entire pathologic process, therefore, apparently shows that the maximum involvement is in the region of the dorsomesial nucleus of the vagus, although some involvement may be seen in almost every part of the neuraxis. The process is definitely an acute parenchymatous degeneration with no evidences of inflammatory reaction. The authors emphasize the fact that the most severe pathologic changes in their cases of experimental poisoning with acid were localized in the same areas in which the grosser morphologic changes are found in an acidotic process in human beings. Dresel and Lewy found in their researches in human diabetes that most severe destructive processes are in the dorsal vagus nucleus and in the globus pallidus. The similarity of the pathologic process in Dresel and Lewy's cases of diabetes and in the experimental cases recorded in this contribution leads Hess and Pollak to believe that the acid might be the genetic factor in diabetes as well as in experimental poisoning with acid, as regards both the nature of the lesions and their localization. The authors also point out that while it has long been known that acidosis increases the irritability of the peripheral nerves, its effect on the central nervous system has, prior to their present work, not been investigated.

KESCHNER, New York.

IMMUNOLOGIC EVIDENCE AS TO THE EVOLUTIONARY RELATIONSHIPS OF MAN. EDITORIAL, J. A. M. A. **85**:1892 (Dec. 12) 1925.

In these days, when anything pertaining to evolution and the species relationships of man has news interest, much attention will probably be paid to a series of articles by Landsteiner and Miller[1] of the Rockefeller Institute on the serologic relationships of the blood of the primates. This topic aroused interest in the early days of immunologic investigation, when the blood relationships of different species, as shown by the new methods, were found to throw much light on the problems of biologic relationship and evolution. Nuttall's famous monograph on blood immunity and blood relationship, published in 1904, brought out the fact that precipitin tests with blood serum from primates showed a close relationship between man and the orang-utan, chimpanzee and gorilla, but less relationship between man and the monkeys. Other investigators obtained similar results and indicated that it was difficult to distinguish between human serum and that of the anthropoids by immunologic tests, but that there are readily discernible quantitative differences between human or anthropoid serum and the serum of the monkeys. Landsteiner, having found that species differentiation is more distinct between corpuscles than between the serum of different animals, has applied this fact to an investigation of the relationships of the corpuscles in the different available primates, studying the effects of agglutinins on corpuscles, and refining the results by determining the effect of removal of nonspecific agglutinins by saturation.

While these and other refined methods fail to differentiate the blood of white men and of American negroes, they do show differences between the corpuscles of human and of anthropoid blood, and between the corpuscles of two genera of monkeys, although the precipitin reaction as ordinarily employed fails to make these distinctions. But it is also clearly shown that the difference between the blood of the lower monkeys and the blood of the anthropoids or of man is much greater than that between the blood of man and that of the anthropoids. Indeed, according to immunologic tests, there seems to be less difference between the blood of man and that of the chimpanzee than between the blood of horses and that of donkeys, which species are so closely related that they can hybridize. This observation agrees with the interesting relationship that has been shown in the metabolism of these species; namely, that while nearly all mammals convert most of the uric acid arising in this metabolism into allantoin, man and the anthropoids differ from other mammals, including the common monkeys, in being unable to do this,[2] because man and the anthropoids alike lack the necessary uricolytic enzyme in their livers.[3] These demonstrations of biochemical relationships are in complete agreement with the view commonly accepted by zoologists that man is not evolved directly from any of the existing species of apes and monkey, which laymen and the fundamentalists continue to assert is the doctrine of evolution, but the monkeys, the anthropoid apes and man have all merely sprung from a common stock, probably at some remote time. The serologic evidence does not indicate that anthropoids are an intermediate step between lower monkeys and man, for man and the anthropoids seem to be equally removed from the monkeys.

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1. Landsteiner, K., and Miller, C. P., Jr.: Serological Studies on the Blood of Primates, J. Exper. Med. **42**:841, 853, 863 (Dec.) 1925.

2. Wiechowski: Prag. med. Wchnschr. **37**:275, 1912. Hunter and Givens: J. Biol. Chem. **13**:371, 1912; **17**:37, 1914.

3. Wells and Caldwell: J. Biol. Chem. **18**:157, 1914.

Study of the natural agglutinins present in the blood of man and of apes shows that the anthropoid blood contains the same four groupings that are familiar in human blood, but that similar iso-agglutinogens are not present in the lower monkeys or in other mammals. To explain this fact, the simplest assumption seems to be that the iso-agglutinable factors existed before man and the anthropoids were differentiated from their common ancestor. Paleontologic studies have led to the generally accepted conclusion that the existing species of man is only one of a number of human species, the rest of which have become extinct, as for instance the Neanderthal man. If the group factors evolved before the human stage had been reached, they must have been present in these various fossil human species. At any event, we now find them present in man, the chimpanzee, the orang-utan, and presumably in the gorilla, which is not at present a laboratory animal, but not at all in the ordinary monkeys.

CHAMBERS, Syracuse.

THE AMPHIBIAN FOREBRAIN. III. THE OPTIC TRACTS AND CENTERS OF AMBLYSTOMA AND THE FROG. C. JUDSON HERRICK, J. Comp. Neurol. **39**:433-489 (Dec. 15) 1925.

Detailed examination of the amphibian optic tracts and their diencephalic and mesencephalic connections shows that *Amblystoma* occupies an instructive intermediate position between the lower urodeles like *Necturus* and the *Anura*. Primordia of most of the mammalian primary optic connections can be recognized, though in very undifferentiated form. In the lower amphibia the various sensory systems of nerve fibers converge into large ill defined correlation fields in which there is little localization of the apparatus of separate movements of the body members — an arrangement adequate for mass reflexes and total body movements, but not well adapted for refined analysis and responses involving rapid and complicated readjustments of the several organs.

As we pass to the higher amphibia these diffuse correlation fields are enlarged and subdivided along functional lines with corresponding elaboration of the action system. The first steps in the process of differentiation of the nucleus diffusus thalami into the mammalian special thalamic nuclei can be observed in the amphibia. This seems to take place primarily under the influence of enlargement of the optic system and elaboration of the motor apparatus.

In *Amblystoma* the subdivision of the diffuse correlation fields is foreshadowed only, chiefly in the form of local condensations of the neuropil of the larger diffuse fields. Each of these denser nuclei receives the larger dendrites of certain neurons of the gray substance and terminals or collaterals of particular functional systems of nerve fibers; but most of the neurons which are here in synaptic relations have also other more diffuse connections, sometimes in very remote parts of the brain. The more refined analysis and localization of function in the correlation centers is incomplete and indeed has not advanced far beyond that seen in *Necturus*.

In the frogs this process is further advanced. In the roof of the midbrain the gray substance is lamellated and the strata are evidently functionally different. This process of stratification has just begun in *Amblystoma* and is scarcely evident in *Necturus*. In the thalamus the central gray, or nucleus diffusus thalami, of lower forms is in part broken up into separate centers and many of the neurons have migrated peripherally into the zone of the primitive white substance to accumulate at the borders of condensations of neuropil of urodele type. This is a neurobiotactic phenomenon and is transitional to the arrangement of compact cell clusters or true cerebral nuclei which is characteristic of reptiles, birds and mammals.

The thalamic connections of the optic tracts are much more extensive than in urodeles and are effected chiefly by fine unmyelinated collaterals of fibers which continue into the midbrain to terminate in the optic tectum. This accounts for the failure of Bellonci and other competent early workers to demonstrate the thalamic optic centers by study of preparations stained for myelin sheaths only.

The basal optic tract of early students is a separate fascicle of fibers from the opposite retina which terminate in a special area of the cerebral peduncle in intimate relations with the oculomotor nucleus. It is comparable with the tractus opticus accessorius posterior (part of the tractus transversus pedunculi) of mammals.

The nucleus of the posterior accessory optic tract is very different in *Urodela* and *Anura*. In *Necturus* and *Amblystoma* it is an elongated area of superficial neuropil which in 1917 was called area lateralis tegmenti and is now regarded as comparable with the nucleus ectomamillaris of other lower vertebrates. Besides the optic fibers, it receives the ascending tertiary visceral and gustatory tract and fibers from several other sources. In the frog this neuropil is apparently separated into several distinct centers, one of which receives the posterior accessory optic tract. This is a small globular cluster of nerve cells in the cerebral peduncle immediately rostrad to the nucleus of the third nerve which evidently corresponds closely with the mammalian nucleus opticus tegmenti of Tsai, or nucleus of the tractus transversus pedunculi.

HERRICK, Chicago.

HEREDITY AND OBESITY. EDITORIAL, J A. M. A. **86**:554 (Feb. 20) 1926.

The statement, frequently encountered, that obesity is merely the expression of an excess of intake of food over the bodily expenditures, is far from satisfactory to a critical student of the subject. There are at least a few obese persons who are fairly active in their habits and frugal in their diets; these, Du Bois[1] remarks, furnish us with the true problem of obesity. A question that obviously presents itself in this connection concerns the basal metabolism of the aberrant types. Do they differ from the normal by carrying out their fundamental exchange of energy more economically? This has been a question not easily answered, because of the difficulties of making tenable comparisons between the different persons concerned.

The obese carry a considerable amount of inactive adipose tissue in their bodies. Consequently, if the metabolism per unit of weight were used as a standard of comparison, the fat person would exhibit a low metabolism. Other modes of comparison also have inherent fallacies. However, when critical regard is directed to these circumstances it appears to be now firmly established that the basal metabolism in obesity is normal—not unduly lowered. The course of the metabolism of plethora, in contrast with the basal exchange, may be somewhat different. It has already been pointed out in *The Journal*[2] that, according to Strouse[3] and his collaborators in Chicago, the obese conserve

1. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lea and Febiger, 1924.

2. The Metabolism in Obesity, editorial, J. A. M. A. **85**:1731 (Nov. 28) 1925.

3. Strouse, Solomon; Wang, C. C., and Dye, M.: Studies on the Metabolism of Obesity, II, Basal Metabolism, Arch. Int. Med. **35**:275 (Sept.) 1924. Wang, C. C.; Strouse, Solomon; and Saunders, A. D.: Studies on the Metabolism of Obesity, III, The Specific Dynamic Action of Food, ibid. **34**:573 (Oct.) 1924; The Metabolism of Obesity, IV, The Distribution of Energy Production After Food, ibid. **36**:397 (Sept.) 1925.

the body fat and thus accumulate more, whereas normal and thin persons use up their food fat instead of storing it. Assuming a peculiarity of metabolism of such a sort, one naturally inquires whether adiposity of the ordinary form is inherited.

Most physiologists are disinclined to admit any hereditary factor in obesity. They insist, with Tileston,[4] for example, on attributing the large incidence of obesity in certain races entirely to their manner of life. This view has been criticized by Davenport.[5] In a statistical inquiry[6] among a large group of families, it appeared that both constitutional and cultural factors play a part in determining abnormalities of build. The constitutional factors may be regarded as not less important in determining the result than the cultural factors. According to Davenport there are at least three biotypes (or elementary species) of human beings in the population of this country characterized by special conditions of build. There is a slender, a medium, and at least one fleshy biotype. In some families there is only one factor, and in others there are two or more factors involved in build. In some cases these idiosyncrasies of build may be due to endocrine idiosyncrasies; in other cases, perhaps, to more general peculiarities of metabolism. These are rather indefinite generalizations on a subject, obesity, that is perhaps discussed by the laity and public press more frequently than any other nutritional disorder. As Du Bois has significantly remarked, the large amount of public interest is in marked contrast to the small amount of scientific information. We do not yet know, he adds, why certain persons grow fat.

CHAMBERS, Syracuse.

THE SUPRARENAL CORTEX AND BODY GROWTH. EXPERIMENTAL RESEARCHES IN CAVIA COBAYA. LUIGI CASTALDI, Arch. ital. di anat. e di embriol. **22**: 297-368, 1926.

In a previous work, whose abstract appeared in the archives, the author gave biometric proof, supported by 11,000 histologic sections, that there is a noticeable correlation between the size of the suprarenal glands and the size of the body. This correlation was more evident during the postnatal than the prenatal period, and was higher for the cortex than for the medulla of the gland. To determine whether this correlation indicates cause and effect, the author extended his investigations by using feeding experiments in *Cavia cobaya*. The results of this investigation give conclusive evidence, for the first time in mammals, of the morphogenetic action exercised by the suprarenal cortex.

Castaldi administered an extract of suprarenal cortex, prepared by himself, to seventy guinea-pigs of different ages. The method of preparation and of administration of the extract is fully described. Control animals were used, and all experiments were conducted under rigidly controlled conditions. The results are fully analyzed and discussed.

The effects of the feedings were: (*a*) On body size and on the general condition of the animals. The author confirms his report to the Academy of Lincei in Rome, that the animals fed with suprarenal cortex reached a body weight greater than that of control animals. He found none of the changes reported by Berman in rats fed with bovine suprarenal cortex: motor agita-

4. Tileston, Wilder, in Barker's Endocrinology and Metabolism, **4**, 1922.

5. Davenport, C. B.: Body Build and Its Inheritance, Washington, Carnegie Institution, 1923.

6. Davenport, C. B., and Nelson, Louise A.: Heredity and Culture as Factors in Body Build, Pub. Health Rep. **40**:2601 (Nov. 27) 1925.

tion, muscular excitability, pugnacity and anger reactions, aggressiveness of the female against the male (suprarenal virilism), changes in sexual desire. (*b*) On the viscera, fat and skeletal muscles. The increase of weight was due to an increase of the muscles, fat and bones, exclusive of the viscera. (*c*) On the blood. Increase of the hemoglobin content and a certain inconstant increase of the cells was found; this effect is to be considered in relation to the improved general condition of the animals. (*d*) On the hair. No modification was found in the pigmentation of the hair, but the length and the rapidity of growth of the hair were influenced by the feeding. (*e*) On the thermogenesis and on teeth. No changes were observed. (*f*) On pregnancy and the products of conception. Animals fed with suprarenal cortex gave birth to larger fetuses. The baby guinea-pigs fed with suprarenal cortex, while drinking milk from mothers fed with suprarenal cortex, were larger than the controls. (*g*) On the skeleton. This chapter is extensive. Figures are given of the lineal measurements of the body with roentgenograms of the whole skeleton, and lineal measurements of the individual bones with their weights, chemical constitution and histologic structure. From the roentgenograms it is evident that the skeletons of the experimental animals are larger and longer than those of the controls. The increase in length is especially pronounced and takes place mostly during the prepuberal period. The skeleton is stimulated to more intensive and more rapid enchondral osteogenesis through proliferation of the intermediary cartilage: but there is also a certain stimulation of periosteal osteogenesis.

The author discusses whether the increased growth is due to hormonic activity or to some other action. He excludes the possibility that it is due to the secretions of certain cells for the use of others in building up protoplasm, the trephones of Carrel, or to proteins contained in the extract, or to the epinephrine contained in most commercial preparations. He concludes that the suprarenal cortex acts on the somatic growth through a morphogenetic secretory property of its cells. This morphogenetic influence, although less definite than that exercised by the thyroid, the hypophysis and perhaps the thymus, has been demonstrated by the author in three ways, biometrically, clinically and experimentally.

NACCARATI, New York.

TOLERANCE TO ALCOHOL. EDITORIAL, J. A. M. A. **86**:488 (Feb. 13) 1926.

The susceptibility of different persons to a drug sometimes shows marked variations; occasionally the same individual exhibits variations in sensitiveness at different periods, owing to changes in his physiologic conditon or to other factors that cannot be evaluated. Such inequalities in susceptibility are by no means identical, however, with what is commonly described in pharmacologic circles as tolerance. The latter is acquired through continued use of the drug, so that an habitual consumer is often able to take without conspicuous characteristic effects quantities that would lead to untoward results in unaccustomed persons. This is notably true of opium and its derivatives; it is likewise familiar in connection with alcohol. Instances are recorded in which steady drinkers have been in the habit of taking alcohol in daily doses exceeding 10 cc. per kilogram of body weight; that is to say, for an adult, no less than 23 ounces of absolute alcohol, or well over 2 pints of whisky at proof, "more than enough to kill a neophyte."[1]

More dependable information regarding the underlying physiologic features of tolerance, and likewise of addiction, is obviously desirable. In the case of

1. Alcohol: Its Action on the Human Organism, London, H. M. Stationery Office, 1918.

alcohol, the evidence remains uncertain. Two possible explanations have predominated. Tolerance conceivably depends on an increased resistance of the body cells to alcohol, an augmented capacity of the organism to dispose of alcohol by oxidation, or both. If there is an increased disposal of the substance, it may be expected that after a given dose the amount present in the blood would not rise to the same level in an habitual drinker as it would reach in the case of a person who had not acquired tolerance. An instance compatible with such an interpretation has lately been described by Hansen of Oslo,[2] in confirmation of earlier indications.[3] Of course, this does not gainsay the possibility of simultaneous increases in cellular immunity against alcohol. According to Pringsheim,[4] a tolerant animal may show few or no signs of intoxication even when its blood contains enough alcohol to cause well marked symptoms in an unaccustomed animal. It is possible, therefore, that when tolerance has become established, either the access of alcohol to the nervous centers is in some way impeded, or, as is more likely, the nerve cells react less readily to its presence.

According to the English students of alcoholism,[1] it seems likely that while the nerve cells of the habitual drinker become tolerant to the presence of alcohol, other body cells are less able to accommodate themselves to it, with the result that they are liable to be injuriously affected, if the development of tolerance in the nervous system leads, as it naturally tends to lead, to the taking of large doses of the drug. That is advanced as a reason why drinkers who have, as they would say, strong heads for liquor and who can consume a great deal of alcohol without becoming drunk are likely to suffer in the long run from some of those bodily disorders characteristic of chronic alcoholism. On the other hand, people who are especially susceptible to the intoxicating action of alcohol are to a great extent protected from excess by that very fact. Just because they are so easily made drunk, they escape the more serious evils of chronic poisoning. Hence, the English writers believe, from the point of view of general health, the acquisition of tolerance really implies the removal of a protective mechanism — it allows the drinker to use the drug in doses which he could not have taken if his brain cells had retained their normal power of reacting to it.

CHAMBERS, Syracuse.

A CASE OF CEREBELLOPONTILE ANGLE TUMOR WITH EXAMINATION OF THE VESTIBULAR APPARATUS, AUTOPSY. FRANK DENNIS, Ann. Otol. Rhin. & Laryngol. **33**:863 (Sept.) 1924.

Dennis states that Jones and Fisher have pointed out that the responses to stimulation of the vestibular apparatus are more characteristic in lesions of the cerebellopontile angle than in other intracranial lesions. The syndrome is: complete deafness on the side of the lesion, lack of responses to stimulation of the vertical semicircular canals of both sides, with good responses from the contralateral horizontal canals. The patient, aged 16, whose case is presented showed signs of brain stem lesion: spontaneous vertical nystagmus upward, staggering, right facial nerve paralysis and bilateral choked disk with

2. Hansen, K.: Experimentelle Untersuchungen über Gewöhnung an Alkohol bei Menschen, Biochem. Ztschr. **160**:291 (July) 1925.

3. Schweisheimer, W.: Deutsches Arch. f. klin. Med. **109**:271, 1913; Inaug. Diss., München-Leipzig, 1913. Gabbe, E.: Deutsches Arch. f. klin. Med. **122**: 81, 1917.

4. Pringsheim, J.: Biochem. Ztschr. **12**:143, 1908.

beginning atrophy on the right. The physical examination revealed: failing hearing and tinnitus; diplopia corrected by glasses; headache; vomiting, projectile in character; failing vision and staggering spells of blindness; difficulty in swallowing, but no choking; loss of control of the muscles of the back, and pain and spasm of the right leg and hip. The neurologic examination revealed: a right facial paralysis; the tongue protruded in the midline with tremor; the reflexes were diminished on the right; there was no Gordon, Oppenheim, Chaddock or Babinski sign; the joint and stereognostic sense was normal. The finger to nose test showed incoordination with both arms. The patient walked with feet apart and lifted the right foot high and in a spastic manner. Bilateral choked disk was present and there was beginning atrophy on the right. The neurologic diagnosis was: right angle tumor. Otologic examination of the ear, nose and throat showed nothing abnormal. A hearing test disclosed deafness of the right ear and a slight degree of obstruction deafness in the left ear.

Vestibular tests: spontaneous, horizontal nystagmus to the right and left on looking right and left; vertical nystagmus upward; crossed past pointing, in the right hand 4 inches (10 cm.) to the left, in the left hand 4 inches to the right. The Romberg test caused marked swaying. Douching at 168 F. of the right ear caused no nystagmus with horizontal or vertical canal and no past pointing with the right arm, but past pointing of 8 inches (20 cm.) to the right with the left arm. Douching of the left ear caused no nystagmus from the left vertical canal; past pointing of 4 inches to the left with the right hand occurred with stimulation of the verticals, and with both hands to the left when the horizontal canal was stimulated. The diagnosis made was: cerebellopontile angle lesion of the right side.

A suboccipital exploration was undertaken and the dura exposed; bulging of the cerebellum was noted, more marked on the right; resistance was also increased on the right, but no tumor was found. The patient died. At necropsy, the skull cap was thin in the parietal region, especially on the right side. The convolutions were flattened, and there was marked increase of fluid in the ventricles. After the brain was removed, a firm smooth tumor, 6.5 by 7.5 cm., was found at the right cerebellopontile angle. The right cerebellar hemisphere was pushed to the left and backward, and the brain stem was displaced to the left. The right acoustic nerve entered the tumor. No adhesions were found between the tumor and the cerebellum. A histologic diagnosis of neurofibroma was made.

Tumors of the acoustic nerve are small. This emphasizes the need for more frequent application of vestibular tests in ear cases, particularly those showing tinnitus and deafness. If this patient could have been examined sooner, vestibular signs of beginning intracranial involvement would have been found, and an examination would have completed the diagnosis by revealing characteristic phenomena of intracranial pressure due to a definite lesion.

FAY, Philadelphia.

MENTAL DISORDERS DURING AND AFTER EPIDEMIC ENCEPHALITIS. V. MÄKELÄ, Helsinski, 1923, 236 pages. Act. Soc. Med. Fennicae, "Duodecim," **4**, Pt. 2.

Twenty-one cases of epidemic encephalitis were investigated to decide whether the mental disorders occurring in the course of this disease are a clinical entity or are related to other psychoses. The variety of symptoms makes it difficult to unify and trace them to a common etiology. In the beginning

of the disease there is a peculiar depression with a general feeling of indisposition, but without localizaton of symptoms. There also are cases of pronounced mania with motor excitement. It is easy to differentiate them, however, from true manic excitement by the absence of euphoria and dissociation of ideas. This period is followed by one of delirium with disorientation as to time, place and persons. In 80 per cent of all cases hallucinations and illusions resembling those of delirium tremens are added; but in epidemic encephalitis the suggestibility is not so marked as in delirium tremens. The perceptive faculties are surprisingly well preserved, as may be demonstrated when the attention of the patients can be fixed during the tests. But there are marked disturbances in the ability to form and combine abstract concepts, which persist for a long time after the encephalitis subsides. A marked lack of memory for numbers and sentences, as well as for events and experiences of former years, was noticed. There was no marked disturbance of consciousness during the delirium and only in a few cases was the author able to detect amentia, which has been more frequently reported by other investigators.

These exogenous psychologic reactions are of minor importance in comparison with the disturbances of energy, emotions, impulses and will, the impairment of which is due to the difficulty of transforming will into action rather than to a lack of will or emotion. Catatonia-like pictures were rarely seen. In schizophrenia the inhibition of muscular action is of psychic origin; in encephalitis it is due to disease of the extrapyramidal system. A depressive type of psychosis predominates. Frequently there are ideas of suicide. Irritability and whining are sometimes replaced by a peculiar indifference to the environment which may even amount to complete lack of emotion. There may be a complete change in the personality. A young patient, normal at the onset of the encephalitis, may present the reactions of a psychopathic child. Attention is diminished without impairment of conception. The ability to form and combine abstract concepts may be well preserved, but with sudden disturbances in the logical sequence of ideas combined with flight of ideas and peculiar aberrations. Very seldom is there lasting impairment of memory, though this is sometimes simulated by fatigue with diminution of mental activity. Somnolence, first emphasized by Economo as characteristic, is not the typical symptom in epidemic encephalitis; the most striking feature is the shifting of sleep to the early hours of the morning and forenoon after preceding periods of unrest. The attempt to localize the lesions responsible for these symptoms was not successful. Cortical disturbances seem to be of minor importance compared to the lesions in the brain stem. There must be a certain constitutional disposition to produce the symptoms described. Susceptibility to exogenous toxic influences is not identical with the disposition for endogenous disturbances as is proved by the differences in behavior in epidemic encephalitis from that in well known endogenous psychoses. The conclusions of the author are based on extensive and carefully carried out psychologic tests. The psychic manifestations in epidemic encephalitis, as the author states, are as manifold as the individual dispositions of the patients.

WEIL, New York.

A CASE OF MULTIPLE HEMANGIOMA OF THE CENTRAL NERVOUS SYSTEM WITH A REMARKABLE CLINICAL COURSE. W. MALAMUD, Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:651 (Aug.) 1925.

The diagnosis and localization of brain tumors are still difficult tasks, and this is especially true of angiomas of the brain. Their growth is so slow as to

produce no great increase in the skull contents, and their tendency to multiplicity renders their diagnosis even more difficult. The patient reported was a woman, aged 39, who came to the hospital because of excitement of an organic nature. She dated her illness back to 1902 when she first noticed numbness in the hands, vertigo and haziness before her eyes. At this time she also had diplopia, severe headaches and pains in the neck. During this time she had periods of excitement, was delirious and had an apoplectic attack, following which she developed a paralysis with ocular palsies. In 1906 she had another apoplectiform attack and was excited, and at this time showed some slowness of speech and paralysis of the left side, and appeared hysterical. She complained continually of her head and neck. Her periods of excitement continued, and in 1909 she had to be removed to a psychopathic hospital on account of her mental state. Here she showed: unequal pupils (the left larger than the right), marked vertical nystagmus, left abducens palsy, left sided nuclear facial paralysis, absent abdominal reflexes, markedly hyperactive left patellar reflex, absent Achilles reflexes, no Babinski sign, no sensory disturbances, scanning speech and a psychic picture of euphoria, depression and apathy. The spinal fluid gave negative findings, and the Wassermann reaction with the fluid and blood was negative. The patient was better for a time, but in 1911 began to complain of pain in the joints and head, and painful sensations in the skin. Auditory hallucinations and compulsive thoughts appeared. In 1913 she complained of vertigo and cramps in the left side. She had an ataxic gait and tended to fall to the left; the nystagmus was hardly noticeable at this time but she had marked scanning of speech. In 1917 she developed olfactory hallucinations, and in 1919 a head tremor almost of parkinsonian character. In 1920 she developed athetosic movements in the fingers of the left hand, generalyzed hyperesthesia and paresthesias and marked gain in weight. She became more and more helpless, and in 1923, about twenty-one years after the onset of symptoms, she died. The clinical diagnosis was "organic disease, apparently multiple sclerosis."

Necropsy showed: a reddish blue mass in the infundibular region of the brain weighing 1,310 Gm. The largest angioma was at the base of the brain in front of the optic chiasm. It lay between the basal ganglia and filled the entire midbrain region. A smaller tumor mass lay in the right pallidum. The second largest tumor mass lay in the pons-medulla region, beginning rostad in the red nucleus and spreading back to include almost the entire pons except the middle cerebellar peduncle and the pyramidal fibers. In addition to these large tumors a number of smaller tumors were scattered through the cortex and medulla of the cerebrum Microscopically there was a picture of an angioma. There was considerable glia proliferation.

The author places the primary tumor in the region of the infundibulum. The peculiar sensations in the hands had their origin in the thalamus, and the apoplectic attacks were due to hemorrhages into the tumors The development of symptoms later in the disease speaks merely for the multiplicity of the lesion.

ALPERS, Philadelphia.

MULTIPLE GANGLIONEUROMATA OF THE BRAIN AND THEIR ORIGIN. MAX BIELSCHOWSKY, J. f. Psychol. u. Neurol. **32**:1-20, 1925.

A laborer, aged 26, developed over a long period of time the general symptoms of increase of intracranial pressure, with bilateral sixth nerve palsies and paresis of the right internal rectus. In the terminal stages the gait became uncertain and ataxia developed to a marked degree. The clinical picture

was that of a tumor in the posterior cranial fossa, but no more exact localization could be made. At necropsy many small tumors were found in the ventricular walls, not only in the lateral but also in the third and fourth ventricles and in the aqueduct. There were, in addition, two larger tumors, both connected with the medulla oblongata. The ventricular tumors projected fairly free in the ventricular spaces but did not break through the subependymal glial layer at any point. In the medullary tumors, the size, structure and growth differentiated them from the other tumors. One was situated in the floor of the fourth ventricle, penetrating into the medulla in a wedge-shaped manner; the other occupied the left cerebellopontile angle and was attached to the medulla, into which it penetrated.

Microscopically, Bielschowsky found even more very small tumors than could be seen with the naked eye. The structure was uniformly the same: the tumors consisted of two layers, a superficial and a deep. In the deeper layer neurocytes were found in various stages of development in addition to well differentiated ganglion cells with vesicular, light-staining nuclei and central nucleoli. A fibrillary structure could be made out in the nuclei. In places there were unripe, frequently multinucleated ganglion cells whose nuclear structure caused the author to place them among the neuroblasts. Occasionally one could see axis cylinders going out from them. Glial elements were also present, showing the morphologic characteristics of normal glial nuclei. Finally, there was an intercellular substance which could only be glial in origin. The outer layer consisted entirely of the same plasma reticulum which formed the groundwork of the deeper layer and contained only a few nuclei.

Bielschowsky believes that these tumors are multiple ependymal ganglioneuromas and that their location is proof of a dysontogenetic condition, since the structure of these tumors compares fairly closely with that of the early embryonal hemispheric cortex. We have in the cell-rich deep zone of the tumor the analog of the nucleus-rich inner plate, while the nucleus-poor outer zone can be identified with the outer cortical layer.

The same reasoning could not be applied to the tumor connected with the medulla and cerebellum in the angle. Both Orzechowski and Marburg have shown the significance of this region for the development of tumors on the basis of embryonic and pathologic-anatomic facts. Marburg called this area the "area parolivaris lateralis." It includes the region between the inferior olive and restiform body. He found under normal conditions in adults remnants in this area, in the form of epithelial and ependymal islands, which formed the starting points of gliomas and atypical formations of a cystic nature. On the basis of Marburg's findings, Bielschowsky believes that even the angle tumor may be developmental in origin, thereby differing in no way in origin from the ventricular tumors.

WINKELMAN, Philadelphia.

ACROMEGALY AND THE SYNDROME OF RAYNAUD. L. VAN BOGAERT and R. DELBEKE, J. de Neurol. et de Psychiat. **9**:511 (Aug.) 1925.

While acromegaly is frankly dependent on a hypophysial disorder, a certain number of clinical characteristics in the disease have been attributed to hyperactivity of the vegetative nervous system in recent years. Abel has recently demonstrated by pharmacodynamic experiments the presence of a hypertensive element in the posterior lobe of the pituitary gland.

The patient whom the authors report had typical evidences of acromegaly, but with no actual symptoms of hypophysial tumor. Nolan Lewis, however, has shown that such cases reveal a pituitary hyperplasia on microscopic

examination. While an enlarged sella turcica is rarely absent with enlargement of the pituitary body (Percy), this patient showed a normal sella. In addition the patient showed a cardiovascular syndrome characterized by marked hypertension without auscultatory signs and with a considerable difference in the pressure in the upper and lower limbs. Raynaud's syndrome was likewise present as shown by painful crises of blanching of the fingers and toes, accompanied by hypesthesia, and relieved by warm water. This association of Raynaud's syndrome with acromegaly presents great biologic interest. While many authors have discussed the rôle of the endocrines in the production of Raynaud's syndrome, few have thought of the possibility of hypophysial disturbance. Claude and Tinel reported a case of Raynaud's syndrome cured for over one year by hypophysial feedings.

The usual pharmacodynamic tests with suprarenal extract, pilocarpine and atropine showed definite evidence of involvement of what the author calls the orthosympathetic and parasympathetic systems. As to the relation of Raynaud's disease to hypophysial troubles, little experimental evidence can be adduced. Pribram obtained relief in two cases of Raynaud's syndrome in two women at the menopause by pituitary therapy. He described another case of Raynaud's syndrome in a patient with a large pituitary tumor. Pituitary feeding gave relief in this case. Pribram looks on these cases as due to endocrine dysfunction relieved by specific therapy. Claude and Tinel, however, look on the action of the gland substance as merely a combating of the neurovegetative dysfunction of Raynaud's syndrome by a regulating agent. In the case reported in this paper, there was no effect on the vessel spasms with pituitary feedings, radiotherapy or pharmacodynamic agents, acting on either the vagotonic or the sympathicotonic mechanisms.

ALPERS, Philadelphia.

PROFESSOR FREUD'S GROUP PSYCHOLOGY AND HIS THEORY OF SUGGESTION. WILLIAM MCDOUGALL, Brit. J. M. Psychol. **5**:14 (May) 1925.

In this article McDougall gives a critical review of Freud's analysis of group psychology as expounded in his "Massenpsychologie und Ich-Analyse." He feels that Freud accepts suggestion as the main factor in group life, which prevents the individual from being free, and which releases all individual inhibitions and lets loose the "cruel, brutal and destructive instincts" — which are stirred to find free gratification. Freud's chief interest is in finding the nature of suggestion. McDougall feels that his own theory of suggestion has been overlooked by Freud. This theory is therefore restated so that a comparison may be made with Freud's. His own theory of mass emotion eliminates suggestion in emotional contagion, and he feels that the display of any instinctive emotion in one provokes a similar emotional response in all — because major instincts are so perceptually organized that such a stimulus in one is sufficient to set the same response going in other members of the group. Suggestion, on the other hand, is explained as the special expression of a submissive instinct, which is evoked by the aggressive behavior of a more dominant individual. Freud feels that love relationships constitute the essence of the group mind and that this relationship turns on the leader. The horde leader of primitive man forced all male members to repress their sexual cravings and forged the bond which tied them to him. This created the illusion that this was a love bond, and the maintenance of this illusion is an essential factor in group life. In leaderless groups an ideal or idea serves the purpose.

The activity of groups today is thus explained by the survival of the influence of the horde father.

McDougall feels that the theory is far fetched, and rebels at explaining all team work, religious activity (church groups) and patriotism on the basis of sexual jealousy and envy. His verdict is "not proved and wildly improbable."

ALLEN, Philadelphia.

POSTNATAL CHANGES IN VASCULARITY IN THE CEREBRAL CORTEX OF THE MALE ALBINO RAT. E. HORNE CRAIGIE, J. Comp. Neurol. **39**:301-324 (Oct. 15) 1925.

In a series of previous studies the relative vascularity of different parts of the brain and spinal cord of the rat has been investigated in the belief that the relative density of the capillary network is a useful index of the probable normal metabolic activity of the corresponding regions. In this paper five areas of the cerebral cortex were similarly studied in specimens of various ages from birth to maturity.

At birth the capillary supply of the cortex is much poorer than at maturity, the germinative layer being richer than any part of the true cortex.

The differences in capillary richness among the various parts are less marked at birth than later in life. There is a slight increase in vascularity in the cerebral cortex during the first five days and a slightly greater increase during the second five days, but this increase is less than that in the brain stem at the same time. Between the tenth and the twenty-first days the vascularity of all parts studied rises rapidly, and the difference between the various layers and the various areas of the cortex in this respect becomes more marked. After twenty-one days the capillary supply continues to increase, but much more slowly, and the differences between various parts become fully established. The changes in vascularity are correlated with changes in the rate of growth, in structural differentiation and in functional activity; and confirmation is obtained for the conclusions previously reached, that the richness of the capillary supply is directly related to functional activity, and that the metabolism involved in the latter requires a greater blood supply than does the metabolism of growth.

HERRICK, Chicago.

DAY BY DAY VARIATIONS IN BASAL METABOLISM OF WOMEN. R. HAFKESBRING and M. E. COLLETT, Am. J. Physiol. **70**:73 (Sept.) 1924.

Careful studies were made of basal metabolism in two apparently normal women. Determinations were made almost daily for a period of four months, totalling ninety-six in one and eighty in the other. A certain variation seems to occur in relation to temperature; the readings in cold weather (from 3 to 10 C.) were found to be about 5 per cent higher than when taken under similar conditions in warm weather (from 20 to 27 C.). Likewise, it was found that during menstruation the basal metabolic rate was relatively low, particularly for the first day or two; just prior to the onset of menstruation a slight rise was uniformly noted, and a minimum rate was observed in the intervals between periods. Increase in rate was observed following sudden noises, in association with anxiety and excitement, and also with mild "digestive upsets," "colds," and pain and discomfort generally. The average variations for the entire observation period were ± 4.4 per cent for one subject and $+5$ per cent

and —6.3 per cent for the other, with maximum variations of + 12.8 per cent and —9.5 per cent and + 18.8 per cent and —14.4 per cent, respectively.

In view of the attention now accorded to metabolic response in relation to various neuropsychiatric conditions, these observations should at least prove of interest and possibly of aid with reference to the proper interpretation of findings in such situations.

RAPHAEL, Ann Arbor, Mich.

THE OPTIC TRACTS AND CENTERS OF THE OPOSSUM, DIDELPHIS VIRGINIANA. CHIAO TSAI, J. Comp. Neurol. **39**:173-216 (Oct.) 1925.

THE DESCENDING TRACTS OF THE THALAMUS AND MIDBRAIN OF THE OPOSSUM, DIDELPHIS VIRGINIANA. CHIAO TSAI, ibid. **39**:217-247 (Oct. 15) 1925.

These two papers form part of an extensive program of research on the morphology of the marsupial brain now in progress in the University of Chicago. In the first paper the distribution in the opossum of the optic tracts in thalamus and midbrain is described, the lateral geniculate body is analyzed, a possible rudiment of the pulvinar is recognized, and special attention is devoted to the most ventral fibers of the optic tracts. These are described as (1) tractus opticus accessorius posterior, whose fibers form part of the tractus peduncularis transversus and terminate in a nucleus opticus tegmenti in close association with the oculomotor nucleus, and (2) tractus opticus accessorius anterior, ending in the corpus subthalamicum.

In the second paper the reflex connections of the midbrain and thalamus are described from the same material. The structure and connections of the mammillary body, habenular nuclei, interpeduncular nucleus and nucleus ruber are reviewed, and the tectospinal tracts and medial longitudinal fasciculus are analyzed.

HERRICK, Chicago.

SPINAL FLUID SYNDROME IN GENERAL PARESIS. B. DUJARDIN, J. de Neurol. et de Psychiat. **9**:497 (Aug.) 1925.

It is easy to distinguish in tabes definite types which have correspondingly definite spinal fluid findings. The same is true in general paresis. According to Claude, this consists in "the homogeneity of all the reactions of the spinal fluid, the intensity of the reaction of the blood Wassermann reaction, the paretic type of colloidal reaction, the lymphocytosis and the increased permeability index (higher than 1/10)." According to the author, however, in this syndrome not all the reactions are of equal importance. "The index of permeability and the colloidal reactions are the most characteristic." Dujardin and Alexander have shown that by a study of the permeability index alone a rational classification of the psychic disorders in syphilitic patients is possible. According to these authors, the characteristics of importance in a paretic spinal fluid not yet affected by treatment are as follows: the amount of antibodies is increased or diminished; the permeability index is greater than 1/10, i. e., increased; the permeability index is not decreased but, on the contrary, is increased by treatment. Studies on the permeability index by other authors have substantiated the claim that it is increased in practically all cases of paresis. The author has followed cases for over six years and has found the index of permeability immutable.

ALPERS, Philadelphia.

RESEARCHES ON GLYCEMIA. I. GLYCEMIA IN EXOPHTHALMIC GOITER AND IN THE NEUROSES AND PSYCHOSES ACCOMPANIED BY THYROIDAL DISTURBANCES. II. GLYCEMIA IN EPILEPTIC PERSONS DURING THE SEIZURES AND DURING THE INTERVALS. FRANCO DI RENZO, Arch. di pat. e clin. med. **4**:405-410, 411-417 (Sept.) 1925.

Among nine patients suffering from exophthalmic goiter, eight were found to show constantly a moderate degree of hyperglycemia. Of six patients suffering from neuroses and psychoses accompanied by thyroidal disturbances, only one, who had a "forme fruste" of exophthalmic goiter showed hyperglycemia. The author thinks that the hyperglycemia found in these patients is dependent on or strictly related to the disturbances of the thyroid secretion.

In twenty-four cases of epilepsy studied during the intervals between seizures the author found a normal glycemic content. In these cases epilepsy was not symptomatic of cerebropathy, because hyperglycemia in cerebropathic subjects is due to the brain lesions. In ten cases examined during the epileptic seizures the author found a constant but transient hyperglycemia, which disappeared a few hours after the attack. He states that the transitory glycosuria sometimes found after an epileptic seizure is probably related to hyperglycemia of high grade; he concludes that hyperglycemia during the epileptic seizure must be related to the sympathetic irritation which exists during the attacks.

NACCARATI, New York.

STUDIES ON THE INNERVATION OF SMOOTH MUSCLE: SPLANCHNIC EFFECTS ON THE LOWER END OF THE ESOPHAGUS AND STOMACH OF THE CAT. H. O. VEACH, J. Physiol. **60**:457-478, 1925.

The suggestion is offered that the chief factor in the production of inhibition of the cat's stomach by stimulation of the sympathetic (splanchnic major) is vasoconstriction. This conclusion is supported by the following evidence: The extent of inhibition parallels the degree of vasoconstriction as indicated by record of blood pressure; if constriction of vessels is slight or absent, the response of the stomach is usually contraction rather than relaxation. Variations in strength and in frequency of stimulation fail to reveal the presence of specific inhibitory fibers in the splanchnic. The action of suprarenal extract on the tonic stomach is inhibitory. When the stomach is contracted in response to stimulation of the splanchnic or of the vagus, epinephrin injection causes relaxation. Anemia from occlusion of the aorta causes relaxation of the stomach; this result is in accord with the work of previous investigators. A few observations indicate that the injection of sodium carbonate into the blood stream results in disappearance of vasoconstriction in response to stimulation of the splanchnic, and that simultaneously the effect of the nerve on the stomach becomes purely motor.

MCCOUCH, Philadelphia.

DEVELOPMENTAL POTENCIES OF PARTS OF THE EARLY BLASTODERM OF THE CHICK. I. THE FIRST APPEARANCE OF THE EYE. LEIGH HOADLEY, J. Exper. Zool. **43**:151 (Jan. 5) 1926.

The degree of differentiation of the optic organ in chorio-allantoic grafts of its primordium or its preprimordial segregation increases as the age of the donor increases. In a graft of the four-hour blastoderm the differentiation of the eye obtained shows only a formation of pigment-bearing cells. In the development of the organ from the anterior portion of the six-hour blastoderm

the pigmented and nonpigmented retinal cells are distinct. In the eight-hour blastoderm transplantation there is a beginning of the stratification which is present in the retina of the normal organ, though the differentiation of the pars lenticularis is not definitely present. The isolated anterior part of the head region of the head-process stage shows a differentiation of the layers of the retina and also of the various regions of the retinal and lenticular zones. By the time the somites are formed, if the optic vesicle be isolated (thirty-three-hour stage) it subsequently behaves as a completely self-differentiating unit.

WYMAN, Boston.

STUDIES ON INTESTINAL INHIBITORY REFLEXES. C. E. KING, Am. J. Physiol. **70**:183 (Sept.) 1924.

These studies were carried out on barbitalized dogs with the registration of the intestinal responses effected by means of balloon tambours. The effects of stimuli from various intrapelvic and cutaneous areas were observed and likewise the results of vagal and splanchnic section and of hypogastric stimulation. King concludes that impulses from the urinary tract, the rectum, the peritoneum, the tip of the nose and the skin of the lower abdomen and perineum produce reflex inhibition with respect to intestinal tonus and motility. The efferent paths for this inhibition seem to occur in the splanchnic system and some of the afferent connections are made apparently through the hypogastrics. The vagus system seemingly was not implicated. King feels also, on the basis of this work, that a partial explanation may thus be offered for the gastro-intestinal disturbances frequently noted clinically in relation to irritative pelvic conditions, and also for the changes in response observed in relation to micturition.

RAPHAEL, Ann Arbor, Mich.

SIZE CHANGES IN PRIMARY BRACHIAL MOTOR NEURONS FOLLOWING LIMB EXCISION IN AMBLYSTOMA EMBRYOS. S. R. DETWILER and RUTH W. LEWIS, J. Comp. Neurol. **39**:291-299 (Oct. 15) 1925.

This investigation is directed to a special phase of the question of effects of functional activity on the histologic structure and size changes in nerve cells. In *Amblystoma* embryos the removal of one or both anterior limb buds results in no decrease in the number of nerve cells in the spinal cord, but there is decrease in the sizes of the motor cells and in the volume of the spinal cord in the affected region. Unilateral excision of the forelimb, prior to the outgrowth of its nerves, is followed by reduction in size of the motor cells of the cord amounting to 8 per cent of their areas in section as estimated with the polar planimeter. Bilateral excision of these limbs results in a similar reduction of areas of the motor cells of 20 per cent. It is concluded that the size of the primary motor neurons is dependent in part on functional connection with the peripheral field and in part on reflex connection with local commissural neurons of the opposite side of the cord.

HERRICK, Chicago.

LABYRINTHINE TYPE OF MULTIPLE SCLEROSIS. J. A. BARRÉ, Rev. d'oto-neuro-ocul. **2**:193 (March) 1924.

In this disease symptoms have heretofore been attributed to the cerebellum which are really of labyrinthine origin. The labryinthine disturbances are more constant and more important than those of the cerebellum, and constitute the

dominant syndrome. Barré reports a case in which there was no cerebellar and practically no pyramidal disturbance, and yet the diagnosis of multiple sclerosis was established by other manifestations, particularly retrobulbar neuritis. The characteristic features were: recurring attacks of vertigo; transient diplopia; nystagmus; head bent to the left; no aberration of tendon reflexes; loss of left plantar reflex; intention tremor. The vertigo was increased by working, bending over or lying down. There was no nausea. Nystagmus was present in all directions of gaze. Cold caloric (17 C.) and rotation tests revealed hypersensibility. Ophthalmic examination revealed a paracentral scotoma and lowered visual acuity, indicating unequal affection of the optic nerves.

DENNIS, Colorado Springs, Colo.

ACTION CURRENTS IN SENSORY NERVE FIBERS (PRELIMINARY COMMUNICATION). E. D. ADRIAN and SYBIL COOPER, J. Physiol. **60**:42, 1925.

Using a three valve amplifier with a capillary electrometer, clear records have been obtained of the action currents of sensory nerves in response to "natural" stimulation of end organs and from motor nerves stimulated reflexly. In this preliminary communication no detailed analysis of results is attempted. Those who have followed the previous papers of Adrian and Cooper on the rate of spinal discharge will welcome this advance in technic which affords a more direct approach to a series of problems whose investigation has been complicated heretofore by indirect inferences of the frequency of afferent impulses and by the assumption of the identity of efferent impulses in nerve and muscle.

McCOUCH, Philadelphia.

OBSERVATIONS UPON THE PERIPHERAL DISTRIBUTION OF THE CRANIAL NERVES OF CERTAIN GANOID FISHES (AMIA, LEPIDOSTEUS, POLYDON, SCAPHIRYNCHUS, AND ACIPENSER). H. W. NORRIS, J. Comp. Neurol. **39**:345-432 (Dec. 15) 1925.

This paper contains an accurate microscopic analysis of the components of the cranial nerves of a number of generalized fishes. A large mass of detail is presented in condensed form with excellent diagrams, all drawn to scale. The results, which cannot well be summarized, will be invaluable for all future students of the nerves of fishes.

HERRICK, Chicago.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Nov. 19, 1925

WILLIAM HEALY, M.D., *President in the Chair*

MALARIA IN THE TREATMENT OF GENERAL PARESIS. DR. H. C. SOLOMON and DR. ARTHUR BERK.

The treatment of general paralysis by the inoculation of malarial blood was first introduced by Professor Wagner von Jauregg, chief of the psychiatric clinic at Vienna, in 1917. However, as early as 1887 he had suggested its use in an article reviewing the literature, "On the Influence of Febrile Diseases on Psychoses." In this article he stated that Hippocrates was acquainted with the art of "healing" of psychoses by febrile diseases and that Galen cited a case of cure of melancholia by intermittent quartan fever. Verga, Gaye, Wille and Sponholz are quoted as not enthusiastic about the matter, but Campbell, Rosenbloom and many more are quoted as favorably impressed with the action of such febrile diseases as typhoid, cholera and intermittent fevers, the acute exanthems, erysipelas, pneumonia, etc., on the psychoses.

With the idea of getting beneficial results from the induction of fever, Wagner von Jauregg began using Koch's old tuberculin for the treatment of general paralysis in 1890, and continued this type of treatment until it was superseded by malaria. The patients were given increasing doses of tuberculin subcutaneously three times a week and allowed to go through from eight to twelve rises in temperature. This was followed by mercury. The course of the disease in these treated cases was compared with the course of an equal number of untreated cases, and it was reported that the length of life of the treated cases was longer and that a greater number of and more lasting remissions occurred. This work was confirmed by Pilcz. In general paralytic patients in whom tuberculin was contraindicated, Besredka's typhoid vaccine was used. This was given intravenously every other day; the same rule was followed as in the tuberculin treatment and very satisfactory results were recorded. Then staphylococcus and streptococcus vaccines were used by him, but the work was given up because the remissions were of short duration. In 1909, Donath of Vienna and Fisher of Prague treated patients with general paralysis by intramuscular injections of sodium nucleinate to produce fever, but this too was abandoned on account of pain, suppuration and no better results. Throughout the course of the various treatments Wagner von Jauregg thought that the best results were obtained in the treated cases that developed an intercurrent febrile disease. This circumstance roused him to the thought of directly producing an artificial infectious disease; with this consideration he turned back to the proposal he made in 1887, and in 1917 nine patients with general paralysis were inoculated with malaria.

Since the institution of malarial treatment certain interesting observations concerning the effect of acute diseases in modifying a chronic disease have been collected. Delgado states that from ancient times it has been the custom of Peruvian natives suffering from uta, a leishmaniasis of the skin and mucous membranes, to repair to certain localities where malaria is endemic, the tradi-

tion being that after a number of attacks of malaria the lesions of uta cicatrize and are cured. Bercovitz states that in countries where syphilis is very common and where malaria is practically universal, as in Indo-China, symptoms of neurosyphilis are rarely observed. This would seem to fall in line with the work of Mathauschek and Pilcz who, in 1913, reported that in their series of 4,134 army officers who acquired syphilis, the anamnesis showed that 241 had an acute infectious disease during the first few years of their specific infection, and of these not one developed general paralysis; on the other hand, of 195 who did develop general paralysis hardly one gave a history of having had an acute infectious disease such as malaria, pneumonia, erysipelas, etc. But Kirschbaum reports that in his clinical material he found ten patients with general paralysis who had malaria during the secondary stages of their specific infection; in our own series there was one such case.

There is no established principle by which the improvement of general paralysis by malaria can be explained. It is based purely on practical experiences and observations, but hypotheses for the action of malaria on general paralysis have been suggested. Plaut proposed the idea of an immunity reaction; that is, that the host infected with malaria produces antibodies or other substances which act against the *Spirochaeta pallida*. Another theory is that the body temperature is the factor chiefly responsible for the favorable effect exerted by the intercurrent infection, and in connection with this the experiments of Weichbrodt and Jahnel are interesting. They found that by placing rabbits infected with syphilis in an oven at a temperature of from 107.6 to 110 F. (42 to 43 C.) for an hour and repeating not less than three times, a complete disappearance and death of spirochetes present in scrotal chancres of the animals resulted. It is known that the spirochete fails to grow at temperatures in excess of from 104 to 106 F. (40 to 41 C.).

Our own series consists of thirty general paralytic patients treated by malarial inoculation; four of them are undergoing treatment at present and, hence, cannot be considered. Of the twenty-six patients, three have died, six have not improved, five show slight improvement, six show moderate improvement and six are apparently definitely improved. It is much too early to place patients in the grouping of complete remissions, moderately good remissions, etc., and we therefore classify them merely as improved or unimproved.

This is only a preliminary report made on account of the prevailing interest in the malarial treatment of general paralysis, and no attempt is made to formulate definite conclusions as to results. However, we are ready to state that our experience seems convincing that the course of general paralysis is definitely modified by malaria and that not a few patients are markedly benefited.

DISCUSSION

DR. C. MORTON SMITH: I have had no personal experience in the application of malaria in the treatment of general paralysis, but some of my patients received the treatment in New York. I saw a man this morning who has taboparesis, but has not had the malarial treatment. He was infected with syphilis in 1904 or 1905 and received mercurial treatment for four years at the hands of an excellent practitioner. He was pronounced cured and in condition to marry, which he did in 1909, and he has three children who are healthy according to his description. His wife has never shown symptoms of the disease. In 1908, four years after his infection, while in the Philippines, he had repeated and severe attacks of malaria. His first intimation that the disease was at all active was three years ago when his Wassermann test, which had been repeatedly negative, became positive. He received a short course of treatment at that time.

The Wassermann reaction became reversed, and his treatment was then interrupted until last year when a lumbar puncture was done which showed a positive fluid, and he received six intraspinous injections of arsphenaminized serum. He still shows a fairly high cell count, a general paralytic colloidal gold curve and strongly positive blood and spinal fluid Wassermann reactions, in spite of the early malaria acquired in the Philippines. It will be interesting to see if there are a greater number of remissions or remissions of longer duration in patients that have been treated with malaria than can be shown with other forms of treatment. The remissions that Dr. Solomon obtained with intensive treatment with intraspinous and intraventricular injections of arsphenaminized serum were quite as striking. I should like to have Dr. Solomon mention one case if he is willing. It is the most striking case with a long remission that I have ever seen. I should also like to inquire if there has been any difficulty in continuing or controlling the paroxysms of malaria. Treatment of general paralysis with malarial inoculation is an extremely interesting subject, but the principle of treating one disease by inoculating living germs of another infectious disease should not be widely applied at present. It is not a procedure devoid of risks. Drs. Solomon and Berk are to be complimented on the fair-minded presentation of this work.

Dr. E. W. Taylor: I should like to ask two questions: First, may we hear from Dr. Solomon about the relative danger in this method, from his experience. Some observers have felt that it was a dangerous method of treatment and that various complications might arise which would not occur under ordinary treatment; the other question is whether or not in the cases that do well there are changes in the spinal fluid.

Dr. Donald Gregg: Are these cases being treated by malaria inoculation alone or is this being carried on in connection with mercury? Is there any relationship between the height of the temperature reaction to the malaria and the tendency toward remission?

Dr. H. C. Solomon: Dr. Smith's first question concerned the spontaneous cessation of paroxysms. This happens not infrequently. A patient will have paroxysms every day or every other day, and then the rises in temperature cease, in spite of the fact that organisms may be found in the blood. We have had this occur a number of times. We have tried to start it up by the injection of boiled milk. We have succeeded a few times in starting paroxysms again by doing this. One or two patients have been given quinine and then reinoculated. One patient was given boiled milk without result; the malaria was then stopped with quinine; he was reinoculated, but paroxysms did not occur until he was given typhoid intravenously, after which the malaria became active again. Dr. Smith asks about one of his patients treated in 1919. This patient made a very good recovery with intraventricular and intraspinal treatments and went back to his position as city engineer in about eight months; his serology is now completely negative. A question that is frequently asked is whether intellectual acuity returns in a remission. We have been checking this by psychometric tests, thus: One man, in 1923, had an intelligence quotient of 59; at the end of a year it was 70, and a year later it was 90. This went along consistently with clinical improvement, and now we have finally succeeded in getting a negative spinal fluid, but it has taken us three years. Dr. Taylor asks about the danger. Malaria is a serious disease. The patients are sometimes very sick as you can well imagine when the patient has a temperature of 106 or 107 F. with tremendous rigors and copious perspiring. Twice we have had to stop the malaria because of jaundice. The linotype operator whom

you have seen had jaundice; therefore the malaria was stopped. Later he was reinoculated, but again it was necessary to stop it because of jaundice. Nearly all patients develop a considerable degree of anemia, but that is of little moment, and in a couple of weeks the blood is back to normal. The condition of the heart has to be taken into consideration. With a temperature of 106 and 107 F., the heart is undergoing a considerable strain. We have selected our patients with some care. We have taken no patients with blood pressure of over 170 and none with marked cardiac lesions or nephritis, and I think that accounts, in part, for the relatively low mortality. One patient did die. He developed hematuria; he had only one paroxysm of malaria, and we stopped it because he was doing so badly. Another patient afforded a good contrast. He was chosen for malaria treatment, but on account of his general condition it was not given. Both died the same day. The first had one paroxysm of malaria; the other had no malaria, and his death could only be considered as the result of general paralysis. The treatment of one patient with hemiplegia was stopped after he had five or six paroxysms, but when he got back in good condition we gave him another course. He has done very well mentally, and while he is not at work he is a very companionable sort of fellow and could go to work. From our own experience we cannot say much about the effect of malaria on the serology because we have been following the malaria by tryparsamide, and therefore what changes we have to report are of no importance because they may have been caused by agents other than the malaria. Bunker and Kirby have not treated patients with drugs afterward. They have followed them up with subsequent lumbar punctures, and they claim marked serologic improvement. The serology does not change much in the first few months, but later, apparently, it does. When a patient has completed the course of malaria we give him quinine and arsphenamine and continue treatment with tryparsamide. Most of the literature on the subject that was mentioned was from 1924, but a great deal of the work reported goes back to 1919 and even before. It still is too early, however, to evaluate these results, and I do not believe any one will attempt to do so now. Only three of our patients had had other types of treatment previously. I do not think that the malaria treatment should be used in general hospitals, because the patients frequently become noisy and disturbed during treatment and need the facilities of a psychiatric hospital. We have used malaria in no other than the general paralytic type of neurosyphilis. In conclusion, I should like to emphasize one or two things. I think it has been clearly demonstrated that the malaria treatment modifies the course of general paralysis. The attempt to cure one disease with another is a new departure in therapeutics. We have treated patients with drugs, chemicals, vaccines and serums, and now finally we come to the consideration of the treatment of one disease by inoculation with another. It does alter the metabolism of patients with general paralysis.

CASE OF APPARENT DETERIORATION WITH ODD BEHAVIOR BUT WITHOUT TRENDS. DR. JULIA DEMING.

This man, aged 24, who comes from a laboring family, is the oldest of six children, all of whom are normal. Delivery was instrumental after thirty-six hours' labor. He did not play as actively as the other children but stayed by himself somewhat. He had pneumonia as a child and "sciatica" in February, 1919. He complained of vague joint pains for five months after this but had, according to the doctor, no fever at this time. He finished grammar school without undue trouble, but at 15 he failed in the first year of high school. After this he had a number of jobs demanding a low type of work such as

mechanics' helper, wood polisher and book carrier in the public library. He is said to have been slow at this work and had difficulty in getting to work on time. He has done no work for two and a half years. He has always been quiet and seclusive, keeping to himself and not going to dances or parties. He went alone to the movies and even skated alone. He took no interest in girls and has shown no sex interest. During the last two years he has been noticed by his family to have been still slower in all movements. He has shown extreme fondness for sweets; in the hospital he occasionally hides cake or bread on his knee at the table. He has been seen by his brother standing in the street staring into space or shaking a fence. He took a clarinet and pawned it for $2. He walked the streets all night on several occasions. A year ago he began showing repetitive movements in eating and dressing, going on with the movements of eating after the plate and cup were empty. He also showed repetition in his speech.

When admitted to the Boston Psychopathic Hospital in February, 1925, he showed fairly frank, cooperative behavior, with repetition in actions and speech. It takes him a very long time to dress, as he makes many uncompleted motions such as reaching for his shoes several times, half putting them on, then taking them off. When he hangs up a garment, he may have it on the hook three times before leaving it there. In eating there are not so many uncompleted actions but he goes on with them after the dishes are empty. He has been noticed to insist on having his shoes at a certain angle before going to bed and has been seen to rearrange the chairs in the ward with special care. He has masturbated but seems to have no conflict over it. He denies having had heterosexual experience. His memory is good; he denies hallucinations and does not tend to distort the external world. He has insight into his peculiar behavior and personality. He says he is shy and embarrassed in a crowd, that he feels that he is not yet a man but will be at 25. He has spoken vaguely and without elaboration of an "influence" over him.

Physically, he shows a dolichocephalic head with small low set ears and a rather heavy under jaw. His tendon reflexes are a little slow; his skin is soft and fine; his hair distribution is male in character. He has a refractive error. His blood pressure is low, systolic 100 and diastolic 65. A roentgenogram of the head shows blood vessel grooves prominent, and sella turcica large and deep but not definitely pathologic. The phalanges show a question of some tufting. A roentgenogram of the chest shows a supracardiac shadow, probably due to a wide aorta as it does not have the usual conformation of the thymus. The blood and spinal fluid Wassermann reactions are negative. The spinal fluid sugar was 0.057 Gm. per hundred cubic centimeters and protein 0.019 Gm. per hundred cubic centimeters. The basal metabolic rate was minus six. A sugar tolerance test showed blood sugar as follows: fasting, 0.086 Gm. per hundred cubic centimeters; one hour after ingestion of 1.75 Gm. of glucose, per kilogram 0.116; two hours, 0.089; and three hours, 0.123. At the time the fourth sample was taken the patient was found eating. His upper teeth have all been removed and three lower teeth show apical abscess. He refuses extraction.

A psychometric test done Feb. 17, 1925, gave him a Stanford mental age of 11 years, 7 months, with an intelligence quotient of 72. He was poor on memory span for digits forward and his memory for visual form was poor. This was repeated April 23, 1925, when he was given a mental age of 13 years, 5 months, with an intelligence quotient of 83. The examiner felt that he showed improvement in his ability to handle constructive thought. Hypnotic suggestion was tried on the patient without results in regard to speech or action.

This man, then, got along fairly well up to the age of 15, carried on at low types of laboring jobs with decreasing efficiency up to the age of 22, became noticeably slow, showed repetition in movements and speech and began to show queer types of behavior such as walking the streets at night, staring into space, shaking a fence and pawning his clarinet which he had previously prized. He gave up work entirely at 23, and is content to sit around home allowing the family to support him. This behavior seems aimless, and to show lack of judgment. No trends have been elicited which might be considered as a driving force. We therefore consider his a case of apparent deterioration with odd behavior but without trends.

DISCUSSION

DR. C. MACFIE CAMPBELL: This case has given us a great deal to think about, and interests us very much. The history shows that the patient had gone along up to 15 years of age after which he took up work outside, when we find him working very slowly, not able to keep his jobs well. Then we find odd behavior; he was sometimes seen for an hour at a time gazing blankly into space. He wandered around at night, wanted to be by himself, and then finally developed a series of odd mannerisms, repetitive movements or compulsive movements, when he did things two or three times, or went through a little ritual in regard to arranging his shoes or fixing the chairs in the wards. What relation has this case to other types of deterioration? The question is, are we dealing with some vague reduction on an organic basis, as yet undemonstrated, or do we have some more subtle undermining psychologic disorder which has not come to the surface in a form that is at all clear? The case is of interest in regard to the whole problem of deterioration in the so-called functional psychoses.

DR. E. W. TAYLOR: Can the patient write any better than he can speak?

DR. DEMING: He has some difficulty at times in getting started, and he writes slowly.

A CASE OF ENDOCRINE DISORDER WITH MENTAL SYMPTOMS. DR. KARL W. BOWMAN.

Mrs. E. K., a white woman, aged 53, a widow, was admitted to the Boston Psychopathic Hospital on March 20, 1925, from the Boston City Hospital with a statement that she was very obese, talked in a peculiar, husky voice and was demented. It has been impossible to obtain a satisfactory history, but the following record is approximately correct. There is nothing of importance in the family history. It is probable that her birth and early development were normal and that she was stout as a child. She did poorly in her studies and barely learned to read and write. She has always been defective mentally and would probably have been classed as a low grade moron. Her menses were established at the age of 14. They were irregular and painful. She was married when 18, and weighed 140 pounds (63.5 Kg.) at that time. When 21 years old, "ovariotomy" was performed at the Massachusetts General Hospital. Since then she has become very stout. It is also said that she has developed mental symptoms, mainly that she has been very suspicious. She has received thyroid medication at various times, often taking 8 grains (0.5 Gm.) daily. In April, 1923, she was studied at the Massachusetts Homeopathic Hospital. There it was felt that the abnormal distribution of fat, the lowered threshold of the tolerance for galactose, and the low basal metabolism all pointed toward a hypergonadism.

Under observation here the patient has been quiet and orderly. She seems happy and talks freely to everyone, showing a very childish behavior. She is disoriented for time and place and shows marked impairment of the intellectual functions. There are auditory hallucinations. There is a history of delusions of persecution, but her statements concerning this are now vague and contradictory. On admission the patient was 5 feet 1 inch (155 cm.) tall and weighed 254½ pounds (115 Kg.). She complained of pain and felt weak so that she spent considerable time in bed. The skin generally was smooth and fairly moist except over the arms and legs where it was somewhat dry and scaly. Beneath the skin were many nodules like a diffuse lipomatosis. There was no axillary hair and very scant pubic hair. On the head the hair was coarse but fairly thick. The voice was hoarse and raucous like a typical myxedema. Some deafness was present in both ears. Blood pressure was 100 systolic and 70 diastolic. Roentgenograms of the skull showed a normal sella turcica. The tips of the terminal phalanges were somewhat tufted. Roentgenograms of the teeth showed two apical abscesses for which she has refused treatment.

The urine has frequently shown a trace of sugar and occasionally albumin and casts. The specific gravity has usually been low rather than high. The blood sugar was 109 mg. The nonprotein nitrogen was 20.8 mg. The blood sugar curve was: fasting, 105 mg.; one hour after glucose, 161 mg.; two hours after glucose, 109 mg.; three hours after glucose, 107 mg. The patient vomited during this test. The basal metabolism was —2 per cent. After ingestion of 40 Gm. of galactose, the urine for the first two hour period showed no reduction; for the second two hour period it showed 0.6 Gm. When she was given 30 Gm. of galactose, the first two hour period showed 0.33 Gm., and the second two hour period gave a positive qualitative test but not sufficient for a quantitative test.

While in the hospital the patient has had periods of fever with no apparent cause, except that on one such occasion there was bronchitis together with a transient heart murmur. There have also been periods when she had small, painful areas of capillary hemorrhage. There have been periods of bleeding from the vagina which at first were thought to be menstruation but later were regarded as hemorrhagic in character. She has had a tremendous appetite. She has been placed on endocrine feeding. From May 30 to June 24, 1925, she was given 10 grains (0.65 Gm.) of whole ovary three times a day with no apparent change in her condition. Since July 3, 1925, she has been fed whole pituitary ten grains three times a day. She has lost 20 pounds (9 Kg.) in weight. Otherwise no special change has been noticed. The blood sugar has shown a marked change, and on October 13 the fasting blood sugar was 206 mg. Four hours after taking 184 Gm. of glucose the blood sugar was 606 mg. Sugar appeared in the urine at this time. On November 19 the fasting blood sugar was 167 mg. The urine has continued to vary; at times sugar is present, at other times it is absent. A blood examination November 19 gave results as follows: hemoglobin, 80 per cent; red cells 3,600,000; white cells 6,200; differential count — polymorphonuclear cells, 53 per cent; small lymphocytes, 36 per cent; large lymphocytes, 6 per cent: transitional cells, 4 per cent; eosinophil cells, 1 per cent; the smears were normal.

The loss of weight, the enormous appetite, the high blood sugar and occasional sugar in the urine all suggest that the patient may be developing a true diabetes. Her condition, otherwise, seems to be on a definite endocrine basis in which the pituitary, the thyroid and the ovaries seem to be involved.

No special benefit, however, has followed feeding with any of these three glands. The patient presents mainly the symptoms of an adiposis dolorosa. Vitaut gives four cardinal symptoms — swelling, pain or tenderness, asthenia and psychic symptoms — all of which are present in this case. Dercum states that the psychic symptoms consist largely of irritability and a feeling that people are against the patient. These are the particular symptoms which have been shown by this patient. Dercum also mentions as other important symptoms the fact that the hearing is often impaired, and that vasomotor symptoms, such as small ecchymoses are frequent. Both of these symptoms are present in this case. Dercum likewise considers that adiposis dolorosa is an endocrine disorder and that four glands may be involved — the thyroid, the gonads, the pituitary and the suprarenals.

DISCUSSION

DR. H. C. SOLOMON: Let me ask about the interpretation of tests for hypergonadism when the ovaries have been removed.

DR. BOWMAN: One reason for making that test was the fact that the report from the Massachusetts General Hospital was not clear. The operation was performed thirty-five years ago, and the record of the case was illegible. It was regarded as an ovariotomy, and from about the time the ovaries were brought to the surface nobody could read what the rest of the record said. While in the hospital the patient has had some periods of bleeding from the vagina which at first, as I stated, was thought to be menstruation but was later regarded as the same kind of hemorrhage she had been having under the skin.

A CASE OF UNSTABLE PERSONALITY WITH VIVID IMAGINATIVE AND DRAMATIZING POWERS. DR. CLEM C. FRY.

The case is that of a farmer boy, aged 16, of Portuguese extraction, who was brought to the Boston Psychopathic Hospital on account of running away from home on several occasions, and cleverly and falsely obtaining money from his father's friends since June, 1925. While under observation here the boy shows, as a rule, fairly normal behavior but gives an interesting account of what he claims to be actual experiences. He also goes through an occasional episode which lasts from a fraction of a minute to fifteen minutes. He tells many fanciful tales of conquest, in which women play the leading rôle; of having intercourse to an excessive degree; of going to dances; of being engaged to the town clerk's daughter; of being in partnership with his father, and of receiving plenty of money to spend. The whole account pictures the patient as the hero. The boy's father states that these are false. The patient tells of other experiences in which his dead mother has appeared to him and advised him. He states that because of his immoral living the devil now appears in place of his mother and his mother comes very rarely. Last May a cow spoke to him saying: "You must leave this barn and never come back here again. You will do well. You are in danger here. Wealth and happiness await you elsewhere." A goat has also spoken to him on several occasions.

The running away is motivated in two ways. He states that often he is unable to control it because something comes over him and he must go. For example, the cow commands him to leave. He also states that he desires to go out into the world to seek adventure and fortune or to be adopted by some wealthy person. As to the cow commanding him to run away we have to think of a retrospective falsification or a very vivid fantasy at the time.

The stealing is to secure money to use on his escapades. He obtains the money by telling tales of his father being in need of funds. He does this very cleverly so that his victims are completely taken in.

We are dealing with a very imaginative youth in a rather drab environment who gives other evidence of his special imaginative powers. This evidence consists in episodes which are always dramatic, but variable in their content and duration, and which may be gradual or sudden in onset and may come on through suggestion. The usual type of episode seen is when the patient wanders about the ward in a dazed state bumping into everything about him. Again, he may assume a very dramatic attitude, often with an appearance of fear and distress. Tears come to his eyes, he crouches and his face and hands tremble. The general appearance is one of a person warding off some horrible danger. After these attacks he tells of having vividly seen the devil beckoning to him. At other times he seems to be passing through some pleasurable experience, and he laughs. He goes through a pantomime of driving a car or playing a baseball game. After these affairs he may or may not be sleepy, he may or may not complain of frontal or temporal headache, and he often drinks large quantities of water.

The boy is physically handicapped by a deformity of the legs and one arm due to anterior poliomyelitis, which occurred at 6 months of age. In addition, he has an unstable personality and an unusual capacity for vivid imagination and ability to dramatize it, thus indulging to excess in romance. He is very suggestible as shown in his reaction to fairy tales, and the attacks which come on if he is talked to about certain things. He shows a tendency to build up fanciful tales of his conquests. Perhaps all this is according to Adler's conception of organ inferiority in which the individual compensates for physical inferiority by living out a life of fantasy instead of reality. On the sexual side is long continued masturbation, homosexual practices and possible sexual experiences with animals. All this is in a person with a poor intellectual endowment. Hysteria might be thought of in this case since the patient is very suggestible, and perhaps not unlike those children who were responsible for the days of witchcraft at Salem in 1692. If he is allowed to go on may we not find this patient developing a purely schizophrenic picture?

DISCUSSION

DR. W. HEALY: I should like to know something more about the patient's background.

DR. FRY: His intelligence seems to be one factor that was noted. In the Stanford examination he was exceptionally good in reasoning power but failed on practically everything else. His environment is poor; he has little chance for recreation.

DR. HEALY: Does he act this way whenever he has an audience?

DR. FRY: If I suggest a girl or the devil, I can usually get him to go into one of these states with or without an audience, but he prefers to have some one around.

DR. HEALY: Does he remember what has taken place?

DR. FRY: At first he could remember everything that went on, but now he says that in the most severe attacks, which last ten or fifteen minutes, his mind has actually been a blank at all times; but at times he tells us what has gone on even when he says his mind has been a blank.

NEW YORK NEUROLOGICAL SOCIETY AND THE SECTION OF NEUROLOGY AND PSYCHIATRY OF THE ACADEMY OF MEDICINE

Joint Meeting, Dec. 8, 1925

CHARLES A. MCKENDREE, M.D., *Chairman of the Section, in the Chair*

CENTENNIAL CELEBRATION OF THE BIRTH OF CHARCOT

CHARCOT AND THE SALPÊTRIÈRE. LT. COL. F. H. GARRISON, Washington, D. C. (by invitation).

Slides were shown exhibiting:

1. Photographs of Charcot taken in 1860 (at the age of 35), 1863, 1872, 1878 and later; also the medallion by Paul Richer, the humorous drawing by Paul Renouard and a portrait of Charcot in the robes of the Paris Medical Faculty.

2. Drawings made by Charcot himself—a caricature of himself and his colleagues of the Paris Medical Faculty in Indian file; a sketch of a patient afflicted with paralysis agitans, and specimens of decorated porcelain.

3. Two views of the Salpêtrière.

4. Picture of Duchenne of Boulogne, whom Charcot regarded as his master in neurology.

5. Pictures of typical hysterical patients at the Salpêtrière.

6. Photographs from the old *Iconographie photographique de la Salpêtrière* (1877-1880), showing the passional ecstatic and cataleptic attitudes which characterized the "major hysteria" of this period. Charcot demonstrated and classified the same symptoms in paintings and drawings of the sixteenth and seventeenth centuries, representing the "possessed" (demonomania). They are also displayed in the bacchantic postures of maenads and corybantes on Greek vases and bas-reliefs.

7. Photographs from the *Nouvelle Iconographie* (1888-1916) showing the facies in exophthalmic goiter, acromegaly, hereditary ataxia (Friedreich) and the muscular dystrophies (the myopathic or amyotrophic face of Marie and Richer); the attitudes and deformations in poliomyelitis, primary lateral sclerosis (spastic paralysis in children), acromegaly (the succulent hand) and paralysis agitans (statue by Paul Richer); also the physical habitus in chronic hereditary trophedema (Henri Meige) and a group of statuary of Paul Richer showing the physical habitus of women in classic antiquity, the early renaissance period and modern times.

An attempt was made to present Charcot as an exemplar of the straight hippocratic trend in medicine (i. e., spontaneous approach to clinical problems without preconceived hypotheses) as contrasted with the tendency toward galenism (superimposition of arbitrary hypotheses on disparate or seemingly unrelated facts) manifest in the later writings of his pupil Freud. In the later phases of the freudian doctrine sex is stressed too much, sometimes to the exclusion of equally potent passions; for example, anger, envy, hatred, revenge, avarice, grief, fear, and other moments of inertia depicted by poets, novelists and observers of human nature generally (i. e., the line taken is not as broad and inclusive as that of Descartes in *Les passions de l'âme*). Freud's Leonardo study of 1916 is a case in point. Leonardo was a splendid

keen-sighted Lombard Italian, handsome, gay and popular in youth, and very like Willibald Pirkheimer, Albrecht Dürer, Lucas Cranach and other doughty humanists of the time, in old age. During the four centuries elapsing since Leonardo's death, no one ever dreamed of saying anything against this great artist who never sought the limelight of publicity. What Freud intimated seems unthinkable, and, were Leonardo alive today, might be regarded as actionable in the pickwickian sense in which Stendhal once brought suit against a man for "attempting his life," i. e., for boring him to death. In like manner, the publication in popular magazines of pictures of Robert Schumann as an example of the pyknic, cyclothymic or manic-depressive type seems a desecration of the fair fame of the well beloved composer, as well as a degradation of the "art and mystery" of medicine. (The author's bibliographic account of Charcot is published in *International Clinics*, **4**:244-272, 1925.)

THE CHARCOT CENTENNIAL IN PARIS. DR. M. ALLEN STARR.

The popular notion of Charcot centers around his studies on hypnotism and hysteria, and Colonel Garrison has called particular attention to those contributions to the functional neuroses; but Charcot was primarily a pathologist, and his work on organic nervous disease was his more important work. This should be emphasized in justice to Charcot, for there is a certain amount of criticism of any one who devotes himself largely to the study of hysteria or to hypnotism. His work during the early part of his career was almost entirely pathologic. His thesis for the doctorate of medicine was on arthritis deformans. His first important contribution was on chronic ulcerative pneumonia. In the first ten years of his career, from 1863 to 1872, his attention was confined almost exclusively to pathologic investigation. Having gone over the large field of pathology, he centered his attention on the pathologic side of the nervous system, because at that time practically nothing was known in regard to the pathologic changes that occur in nervous diseases.

Any treatise on the practice of medicine published in 1875 mentions only three diseases of the spinal cord: myelitis, locomotor ataxia and anterior poliomyelitis. Charcot began his work in the pathology of the nervous system in 1872, and continued it from that time on. The important work that he did was pathologic, and it was largely in connection with the pathology of the spinal cord and the brain that he made his reputation. In 1872, 1874 and 1876, wonderful investigations were published by Fritsch and Hitzig in Berlin and by Ferrier in London on the localization of functions in the brain, and in the following year Charcot made important contributions to the subject.

I was a student of Charcot in 1882, and I saw only one case of hysteria demonstrated in that whole semester. He discussed brain tumors and aphasia, and word blindness and word deafness, drawing those diagrams of the brain with which we are all now familiar. I think this side of his life should be emphasized.

I will now give you an account of the proceedings in Paris in May. The French government, unlike our own, takes an interest in scientific progress and in her scientific men. The government has dignified the memory of her men by proper memorials; during their lifetime by decorations; after death their memory has been perpetuated. The governmental celebration of the one hundredth anniversary of the birth of Charcot was made at the instigation of the Academy of Medicine of Paris and the Society of Neurology of Paris. Invitations were sent to nineteen countries, and eighteen of them sent official delegates to the city of Paris in the month of May. The Society of

Neurology particularly designated certain gentlemen who happened to be members of their body. From this city were invited Dr. Sachs, Dr. Hunt, Dr. Dana and myself, all of us honorary members of their society. I was the only one able to attend. Seven hundred physicians gathered from all parts of the world. On the first two days of the congress the scientific meetings were held at the Salpêtrière, from 9 to 12 and from 3 to 6. The first day was given over to the consideration of what is known as Charcot's disease, amyotrophic lateral sclerosis. The pathology was described by Marinesco; the clinical history was discussed by Christiansen of Stockholm and Winkler of Amsterdam. The second day was given over to the study of migraine, to which Charcot had made some contribution. This was dealt with by Neri of Rome and by the younger Pasteur. Those were the two scientific meetings of the congress.

Official meetings were held by the French government. The first was very impressive. It took place in the great hall of the Sorbonne, which holds 3,000. The president of the French Republic entered with a band from the national guard playing the Marseillaise, escorted by the hussars, each man over 6 feet 4 inches tall. The president and the minister of education presided. The latter made a charming address, and introduced Babinski, the first successor of Charcot in the chair of nervous diseases at the Salpêtrière. Babinski read an interesting address describing Charcot's personality, with many details of his life. This was followed by the presentation of their credentials by the delegates of the various countries represented. It was thought best not to have eighteen different addresses, and a representative was selected from among the delegates, Marinesco, a particularly interesting and eloquent old gentleman being chosen, with Winkler of Amsterdam to represent the various universities sending delegates. Sir Robert Sinclair, the representative of the Royal Society of London, also made an address. It was altogether a very brilliant occasion. The speeches were interspersed with music.

The next official celebration was on the following day at the Academy of Medicine. Pierre Marie, as the second successor of Charcot after Babinski, delivered an address full of feeling, inspired by his deep personal attachment to his old professor; it contained an intimate note which deeply moved the emotions of every man in the room.

The third occasion of interest was the banquet, which was attended by 700 guests. Speeches were made by the minister of education and by the various delegates, each being called on in turn to make a short address. Almost every delegate not only alluded to Charcot and his work, but also made some reference to Charcot's family, for at the center of the table sat his son Commander Charcot, a member of the navy, who, although educated as a physician much to the distress of Charcot gave up the practice of medicine. He has made a world wide reputation as an investigator of the arctic and antarctic regions. He was the first to approach the south pole before Shackleton actually reached this point. At the end of the addresses Commander Charcot delivered a most touching speech, thanking everyone for the homage paid his father, and gave a delightful picture of his father's family life which of course no one else would have been able to do; as the culmination of his address, he invited the delegates to tea at his father's house at Neuilly on the following afternoon. At this function, we were received by Charcot's son and daughters. The library is much as Charcot left it, and is decorated by frescoes made by his hand; the tiles about the mantle were painted by him.

The last reception was given by the city of Paris at the Hotel de Ville at 4 in the afternoon. The mayor of Paris was present. At the close of the

meeting a medal was presented which had been struck off in commemoration of the centenary of the birth of Charcot. As a celebration it was an enormous success. I think it is a great source of inspiration for a government to recognize in such an official manner the centenary of one of its greatest men.

CHARCOT, THE DIAGNOSTICIAN AND HYPNOTIST. DR. BERNARD SACHS.

Charcot was above all things the great diagnostician. I think I can fulfil the purpose of the evening best if I give you some personal impressions of Charcot as a teacher at the time when he was at the zenith of his scientific career. Dr. Starr and I are the only ones in this room old enough to claim that they were students under Charcot. Starr and I sat together on the benches under Meynert, with Freud as our neighbor. I reached Paris in the spring of 1883, Dr. Starr being a little ahead of me. Let me recall to your minds that at that time the guiding spirits in neurology were: in Germany, Leyden, Erb, Strümpell, Flechsig, Nothnagel and Wernicke; in Great Britain, Hughlings Jackson, Byron Bramwell and Ferrier; in America, Weir Mitchell, Beard, the elder Hammond and Seguin. In France, only one name dominated the entire field of neurology, and yet Charcot was surrounded by a brilliant group of younger men. During the years from 1880 to 1893, in France there was not a book published on any neurologic subject that was not either dedicated to "mon maitre, Charcot," or written at the inspiration of Charcot. The pre-eminence which Charcot enjoyed at that time was deserved, if ever any man deserved to be the master of an entire science.

Coming as I did from the laboratory of Meynert, great anatomist but rather poor teacher that he was, it was a privilege to sit at the feet of a man like Charcot, who was the most inspiring of clinical teachers. He had a way of making the most uninteresting fact in medicine fascinating. I can recall his napoleonic head, his classic features, his beautiful hair as he sat during the lecture surrounded by his group of assistants. A good many of the men who had graduated from the clinic itself continued to attend almost every clinic that Charcot held, and particularly those famous Tuesday morning clinics. A foreign student was admitted to the clinic without trouble, and easily fell in with the group of men from every corner of the globe who were content to listen to the oracle. At the time I went to Charcot for instruction in neurology, he was the great exponent of organic neurology. Like most neurologists of that time he graduated from the ranks of the internists and the pathologists. The work for which Charcot was already famous was on tabes, on the amyotrophies, on the progressive muscular dystrophies and on disseminated sclerosis. The differential diagnosis between paralysis agitans and disseminated sclerosis was due to his clinical acumen. Then there was his work on poliomyelitis, myelitis, and above all, the subject that so many of us were interested in, the study of cerebral localization.

I remember one special occurrence, and it was this I had in mind when I said I was going to speak of Charcot as a diagnostician. While discoursing on cerebral localization he brought in a patient who had been chief flutist in one of the Paris orchestras. He presented the man to show the loss of one special function. The patient said he came to consult Charcot because he could no longer pout his lips in a way to produce a perfectly pure note on the flute. Charcot said it was the finest example of localization of function that we could possibly have. He said, "But it is not due to any cortical trouble, such as you have been thinking of. That man has no tumor. That is the first stage of a general paresis. It is this man's most highly specialized function,

and it is the first to go." It was by that method of clinical contrasts that he had a way of impressing his students and of making his lectures dramatic to a degree.

I can also bear witness to the fact that during the year I was there, hypnotism did not play the rôle that it was supposed to have played in Charcot's clinic. Before referring to hypnotism, it is necessary to speak of the work on hysteria. When we, as students, went to Charcot to study hysteria, we went there under the impression that it was very marvellous that a man who had all his life devoted his time to organic neurology should begin to devote himself to the neuroses. I remember his presenting some extraordinarily interesting cases of hysteria. Charcot, however, was bent on finding the analogy between hysteria and organic disease. It may seem queer to us at this day that whenever he spoke of hysterical hemianesthesia he was constantly trying to find what actually happened in the brain to bring about such a condition. In his lectures on hemianesthesia he finally stated that he did not know what the underlying changes were. We were under the impression, as students under Kussmaul and Leyden, that there was something strange about the occurrences in Charcot's hysteria wards. Every one had doubts as to whether the thing was not manufactured in Paris for special French use. It is perfectly true that the things seen at the Salpêtrière were not to be seen anywhere else. I remember the following incident: it was after one of his lectures on hysteria that the entire class was taken up into one of the small wards, in which there were twelve or fifteen women patients. Some of the students were on one side, and the assistants on the other, and it happened that a passage was made for Charcot to pass through the middle. The moment he was seen by the patients in that ward, the entire ward fell into a hypnotic state, every patient presenting some form of hypnotic trance. In some of the universities in Germany it was said that such occurrences were all prepared, and that Charcot trained his material so that they did anything he pleased. Charcot at that time was aware of the fact that there was no deception about this, but his personality and his relation to the patients were such that his appearance acted as a powerful suggestion, of which the hypnotic state was the result. Charcot tried in every instance to reveal the cause of the hysteria. One of the most interesting cases he has published is an entire chapter, or perhaps two, on hysterical anuria. He proves conclusively, even to the reader of the present day, that there is such a condition as hysterical anuria. His argument shows that in studying hysteria he was chiefly interested in determining what brought about the hysteria. The original psychic shock in the case of hysterical anuria was experienced at the time when the patient had fallen into an open fire; from this time on, she developed the hysterical complications. The whole subject of hysteria was treated by him in such a purely scientific manner in its relationship to organic disease that we can well afford to accept many of the explanations Charcot gave us of these hysterical phenomena. Only one circumstance challenges criticism. Many of the patients were detained for from ten to twenty years at the Salpêtrière. Evidently, in the majority of cases no serious attempt was made to cure them. This was due surely to the fact that Charcot and his followers wished to retain them as good clinical material for teaching.

Let me add just one word that is true not only of Charcot and his influence as a teacher, but also of the entire French manner of handling the subject of neurologic education. Pierre Marie at present, a most delightful successor to Charcot, sees every patient in person in the outpatient department. There

is much more to learn about nervous disease from outpatient work than from hospital work. That is also true of a good many other diseases. The man who studies heart disease in a hospital ward will not learn as much of the origin of the heart disease as the man who sees dozens of early cases in the outdoor clinic. The importance attached to the outpatient work in France is accentuated in the neurologic education, and I think we can well afford to emulate that example by making the outpatient neurologic department an integral part of the hospital division.

The Neurological Society and the Neurological Section of the New York Academy of Medicine have done well in realizing the services rendered by Charcot and in doing reverence to the memory of the greatest master mind in neurology.

DISCUSSION

Dr. M. Allen Starr: The famous Tuesday morning lectures were held in a long, narrow hall with benches rising from the floor. After the audience had gathered on these benches, the side windows were closed by shutters so that the room was in complete darkness. There was a stage at one end, and the footlights were turned on. Charcot entered from the side with a number of his assistants, and seated himself at a little table which did not face the audience, but faced across toward the stage. Then an assistant brought the patient in and placed him in front of the footlights; the calcium light from the other side was flashed on him, so that he was the center of the only light in the room. Then Charcot began to discuss the case and to read the history, and the students could see everything that he wanted them to see. If it was a patient with shaking palsy he was put in the limelight, and soon other patients with tremor were brought in and placed along the footlights so that we could see the different kinds of tremor. The patients were then ushered out, the footlights put out, and lantern slides flashed on the screen to show the lesion, so that the symptomatology, the diagnosis and the lesion were all before the students. That was a dramatic clinic. Some people criticized it as being too dramatic, but it taught the student.

Charcot and the Arts. Dr. Charles L. Dana.

Dr. Dana, who because of illness was unable to be present, sent to the academy a large collection of pictures for projection. These were shown, with running comments by Dr. Jelliffe and Colonel Garrison. Dr. Dana's pictures showed particularly a phase of Charcot's artistic taste, his study of the products of great artists who had depicted various striking symptoms of disease and early surgical procedure. Projectoscopic illustrations were shown of portraiture of disease by Dürer, de la Robbia, Rembrandt, Rubens, Velasquez, Teniers, Jr., Brueghel and others, chiefly Dutch, Flemish and Austrian artists.

DISCUSSION

Dr. Smith Ely Jelliffe: I had the pleasure of listening to Charcot in 1891 in the lecture room Dr. Starr has so well described; I have also known personally all of the successors to the chair after Charcot's death.

In reference to Dr. Dana's pictures, Charcot had gathered together many illustrations of a vast majority of facial contortions, bodily postures, etc., which proved the influence of the emotions on bodily movement. As Sherrington has reminded us, "emote" is the root of the word, meaning that bodily movement is but an emoting of feeling. Perhaps the popular folksong "Every little

movement has a feeling all its own" contained more science than one was apt to attribute to it. The studies of Darwin, on *The Expression of the Emotions in Man and Animals,* and that of Hughes, on *Mimicry in Man,* are classic texts. Some of the neck position, and "Stellreflexe" described by Magnus and de Kleijn, were illustrated; and certain psychotic, catatonic and other attitudes were related to the psychologic states which permitted such emoting.

NOTE.—Charcot mementoes, photographs and literature have been on exhibition at the New York Academy of Medicine for several months.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 17, 1925

SANGER BROWN, M.D., *President, in the Chair*

POSTENCEPHALITIC OBESITY. DR. THOMAS G. WALSH.

This article will be published in a later issue of the ARCHIVES.

NONBIFURCATING NERVE FIBERS OF THE TRIGEMINAL NERVE. DR. WILLIAM F. WINDLE.

Golgi preparations of the brains of new-born mice and fetal pigs reveal several types of nerve fibers in the sensory division of the trigeminal nerve. The well known bifurcating fibers are clearly demonstrated. Besides these there are ascending nonbifurcating fibers terminating in the main sensory nucleus, and descending nonbifurcating fibers terminating in the nucleus of the spinal tract. The bifurcating fibers terminate in both nuclei and are usually of larger caliber than the descending nonbifurcating variety.

There is reason to believe that both the bifurcating fibers and the ascending nonbifurcating fibers carry tactile impulses to the main sensory nucleus and the nucleus of the spinal tract. It is also probable that the descending nonbifurcating fibers carry painful impulses to the nucleus of the spinal tract only.

DISCUSSION

DR. G. B. HASSIN: Did Dr. Windle make his studies on embryos or new-born animals? Ramón y Cajal found trigeminal fiber bifurcations only in new-born mice. He pointed out that the ascending branches are considerably thinner than the descending ones, both giving off numerous collaterals. Is it possible to explain the apparent or real absence, in older animals, of the thin ascending branches by the time element, that is, by their regression in the course of the animal's growth, or by other factors?

DR. L. J. POLLOCK: I would like to express the great pleasure I have had in listening to this interesting approach to an explanation of an obscure physiologic condition. In sensation we deal with a function much of which to date remains obscure despite a large amount of research. The literature is full of misinterpretations whether dealing with the peripheral nervous system or the intraspinal pathways or lower or upper levels of sensory representation. It is particularly interesting and refreshing to know that we have a method of approach to an accurate study which will explain certain clinical observations. The sum total of our knowledge does not explain all of our clinical findings. It is, for example, very difficult to explain many things dealing with intraspinous pathways in tabes dorsalis. It is difficult to attribute the dissociated

sensory loss to phylogeneses. Similarly, in cases of posterior root section it is difficult to explain the preservation of large areas of touch purely on the basis of overlap. It is difficult to explain why, in posterior root section, we cannot uniformly destroy the subcutaneous pains that occur in tabetic crises or some of the deep boring pains that occur in other diseases or injuries. Possibly that type of pain is subserved by fibers entering the cord through the anterior roots as suggested by Shaw.

THE MECHANISM OF STAMMERING AND STUTTERING. DR. MEYER SOLOMON.

My views are based on the study of other stutterers and stammerers, both children and adults, as well as my own personal experience. I employ the terms "stuttering" and "stammering" synonymously for the transient, intermittent speech disorder which is characterized by a break in the rhythm of speech in one or more portions of the speech apparatus anywhere from the lips to the diaphragm. By mechanism I mean the sequential order in which the phenomena take place. There are two fundamental problems: 1. Of the two types, central and peripheral, of phenomena present, which are primary and which secondary? 2. What is the origin and nature of each type of phenomena?

After classifying the past and current theories and the inducing causes of onset, and admitting the possibility of the existence of inherited, congenital or acquired instability of the speech centers, cortical or medullary, I contend that a state of nervous and mental excitability is preliminary to stuttering, which is not merely a speech defect but also a personality problem with instability of reaction in general, especially in social relations requiring speech.

In the developed case there is the following sequence of events:

1. First, there is a preliminary, antecedent and causative nervous and mental attitude of excitability or emotionalism, characterized by general overanxiety, intensity and enthusiasm, with an excessive sense of responsibility for the task, especially in social relations requiring speech. There is impulsiveness, explosiveness and impatience, with a desire for the immediacy of speech expression, with undue hurry and rush, so that the stutterer may endeavor to say a whole syllable, word, sentence, paragraph or story with a single effort and from the very first position assumed by the speech apparatus.

2. Multiple ideas and tendencies to bodily movement, especially for speech expression in social relations, start out simultaneously. This, with a failure to inhibit an impulse after it has found partial expression, plus an undue tendency to develop skeletal tensions in other difficult responses as well as speech, eventuates in conflict and rivalry of thought processes and impulses competing for the final common pathway through the lower centers of speech. Mental chaos and discord thus precede and produce speech chaos and discord.

3. The resulting disorder in the peripheral speech machinery is characterized by hypertension, spasm, incoordination or disharmony between its different divisions (oral, laryngeal and respiratory). Two main faults result: (*a*) inability to produce any sound at all, due to the assumption of the position of deep inspiration or deep expiration, holding it and endeavoring to produce sound from either of these positions — an impossibility for any person; (*b*) normal production of the initial sound of a syllable and repetition of same because of inability to advance to the next sound, be it consonant or vowel, due to the effort to produce the second sound from the same position from which the first sound was produced — another impossibility for any human being. Fundamental in both instances is the insistence on producing sounds

from positions of the speech apparatus from which it is impossible for any one to produce them.

4. Complicating mental after-effects during speech result, and are themselves independent causes producing phases 1, 2 and 3. When in speech block or distress, mental confusion (with bewilderment, flurry and daze), self-consciousness (with embarrassment and shame) and fear occur, they increase the tendency to hurry and rush, the conflict of multiple impulses and speech disorder.

5. Personality transformation, of four main types, gradually occurs: (*a*) suppression of the personality (excessive self-consciousness, fear, lack of confidence in one's self and speech organs, timidity, self-isolation, etc.) — the shut-in type; (*b*) over-assertiveness; (*c*) indifference; (*d*) common sense attitude, with constructive efforts for gradual improvement and recovery.

Bugaboo sounds, syllables, words or social situations, associated with undue anxiety and fear, are due not to some peculiar suppressed wish, but to association or conditioned emotional reflexes dependent on the memory of past and fear of oncoming difficulties and failures. Mental conflicts are of significance in three main ways: (*a*) they may increase the general instability and tendency to hurry and rush in speech; (*b*) they are centered about bugaboo sounds, syllables, words or situations; (*c*) they revolve about superadded mental states and personality reactions mentioned in phases 4 and 5.

Any treatment which does not consider all the five factors enumerated is not thorough or based on fundamentals.

DISCUSSION

Dr. E. L. Kenyon: I find myself agreeing with Dr. Solomon on the mental side of the disorder, but disagreeing with him rather completely on the peripheral side. Consequently, I find my conception of the mechanism of stammering, taking the disorder from the beginning in childhood along to maturity and as a whole, not entirely in agreement.

If we are ever to arrive at a complete understanding of the mechanism of stammering, we must bear in mind that the phenomenon possesses two distinct phases, one mental and the other peripheral. We must also bear in mind that the mental phenomena are to be clearly differentiated into that which was present at the time the stammering began, and was, therefore, presumably causal in character; and the mental phenomena that were not present at the incitation of the stammering and have developed evidently in large part as a consequence of the social struggles of the sufferer.

Both the peculiarly disturbed behavior of the physical machine itself, and the mental disturbance immediately responsible for the peripheral wrongness of action, in my judgment, remain as yet unexplained. The only phase of stammering which is now quite definitely understood is that made up of the general psychologic phenomena which are chiefly the result, rather than the cause, of the stammering, but which form a more or less conspicuous part of the diagnostic picture of most older sufferers.

The child, aged from 3 to 6 or more years, starts lightly to stammer; the reason, in any adequate sense, is as yet one of the mysteries of the disorder. Usually, by the time he has become 15 years of age, under the stress of persistent and distressing social experiences, he has become psychologically filled with fears, excitements, emotions and tensions.

A number of years ago, in America and elsewhere, psychologists, neurologists and psychanalysts, following the earlier footsteps of Denhardt, Liebman

and others, also took up this problem. In the United States the movement was headed by Dr. Smiley Blanton. Much valuable knowledge concerning the general psychologic disturbances of stammering, chiefly, as I have said, resultant rather than causal in character, has been added to the subject. I know of no one more intelligent in presenting this phase of the disorder than our essayist, Dr. Solomon. Nevertheless, I cannot feel that this class of investigation is now leading to, or is likely to lead to, an actual understanding of the fundamental phenomena of this puzzling disorder. The thought of this class of investigators has concerned itself rather with the complications of stammering than with the actual disorder itself. They seem to be circling rather closely around, than moving directly toward, the heart of the stammering mystery. I make this statement with full knowledge and full credit for the direct light thrown on the subject by the studies of behavioristic psychology in children.

In what direction, then, does the heart of the stammering mystery lie? It lies in that direction which leads to an explanation of the peculiarities of the peripheral disturbance. In all efforts to arrive at an understanding of the phenomena of stammering, the psychomuscular origin and the physiology of the speech machine has, up to this time, been left out of detailed consideration. And, in view of the fact that an understanding of the psychologic processes that control this complex muscular function must depend on an understanding of the function itself, it follows that the psychology of speech movements has not yet been adequately studied. Yet I venture to prophesy that the peculiar mechanism of this extraordinary disorder will be found to involve a disturbance in the psychologic control of speech movements, coupled with a certain peculiar susceptibility of the speech machine to occasion disaster in talking.

The following considerations will help to bring out this point of view: all the general psychologic disturbances present in the stammerer are not uncommonly present in like degree in the nonstammerer; muscular tensions in the peripheral speech area, fully as severe as those of the stammerer, are present in certain other disorders of speech, but without the characteristic hesitations of stammering. Such are dysphonia spastica and the tension speech disorders present in certain neurasthenic persons, and even the severe stammerer is almost invariably able to sing without hesitation. It is interesting that the disorder has never been known to develop among deaf-mutes who have been taught to talk.

It is dangerous to monkey with the buzzsaw of speech. The buzzsaw is the action of the vocal cords themselves. The linear difference between the ability of the vocal cords to vibrate, and the impossibility of their vibration, is only a distance of 1 mm. or less. If the speech machine is set going with that kind of disturbed direction which permits the vocal cords to close together, instead of alining themselves 1 mm. apart, the production of voice must be completely blocked. The hesitations of speech that are determinative of the peculiar disorder we call stammering are not, in my opinion, due chiefly, as is universally taught, to muscular tensions as such, but to that kind of disturbed guiding mental activity that causes the vocal cords to take not the normal position for talking, but rather a completely closed approximation that prevents talking. The muscular tensions, as such, in the speech regions are not primarily responsible for the hesitations of stammering, but are, for the larger part, the result of a struggle due to wrong vocal cord action coupled with habit.

How large a part of this disturbance in the cerebral motor area, speaking now of the very inception of the disorder, may be due to general nervousness and emotionality; and what other factors may enter such disturbance at this earlier period must be left for later discussion.

(By imitation and description, using illustrations of different types of stammering, Dr. Kenyon pointed out the fact of vocal cord closure during the talking struggle, compared certain types of stammering to laughter and coughing, and pointed out that the only possible explanation seemed to be a disturbance in the action of the motor speech areas. He also spoke highly of Dr. Solomon's presentation.)

DR. A. B. YUDELSON: I would like to ask Dr. Solomon whether he noticed that the greatest difficulty that stammerers experience is in uttering the labial and glossal consonants and if so, what explanation he offers.

DR. JOHN FAVILL: In what way does Dr. Solomon account for stammering by people reading a paper before an audience, under which conditions there cannot be a multiplicity of ideas or a conflict of thought because reading is often a rather reflex affair from the eye to the speech producing mechanism? Many of us can read aloud without knowing what we are reading. How many stammerers show a difference under those conditions?

DR. MEYER SOLOMON: In answer to Dr. Favill, some stutterers do better when reading aloud than when not. Others are better when speaking than when reading aloud, because they take time and feel more at ease. When reading aloud some do not feel at ease because they are watching for difficult or bugaboo words and so do not live in their thoughts or feel calm. On the other hand, you find some who are better when reading aloud than when speaking freely. I find frequently in children that when speaking they are in such a hurry that they endeavor to say all they have to say almost in a single effort, whereas when they read aloud they feel that all there is to do is to go ahead and read the words quietly. Whether one is better when reading aloud or speaking depends on the attitude or mental state.

Dr. Yudelson asked why there is more trouble with the labial and glossal consonants. The explanation is that the labials and glossals are more difficult for the average person and, consequently, even more so for the stutterer.

Concerning Dr. Kenyon's discussion, many writers have maintained that there is an instability of the speech centers or speech mechanism. That may well be true. But that alone would not explain stuttering, since, when the stutterer speaks calmly and lives what he says, he has no trouble. It is my contention that it is the emotional attitude of the person at the time he is speaking or reading which is the fundamental thing, even though there may be an instability of the speech centers, peripheral or central. Even if one could prove that there is an inherited instability of the speech centers, stuttering is, nevertheless, preventable and curable if the emotional attitude is one of poise.

As to why a stammerer can sing without speech difficulty, I believe the explanation is in the fact that in singing one must live in the song and so think and speak rhythmically.

The central origin of stuttering should be stressed as much as possible, and especially its nervous and mental aspect. The fact is that neuropsychiatrists have neglected this important condition to a large degree. With a better neuropsychiatric approach, I am sure the problem will be handled in a more satisfactory manner in the future than it has in the past.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 18, 1925

SHERMAN F. GILPIN, M.D., *President, in the Chair*

A PATIENT PRESENTING SUBJECTIVE AND OBJECTIVE SENSORY DISTURBANCES IN A SEGMENT OF A LIMB. DR. ALFRED GORDON.

A white, married woman, aged 35, has suffered from deep seated pain in her right arm for fifteen months; she describes it as boring, burning, pulling or pressing, and frequently it interferes with her sleep. When the pain first made its appearance she noticed weakness in the right upper limb. The past medical history is unimportant except for an operation for removal of a uterine neoplasm.

Examination.—In addition to the continuous pain, confined exclusively to the arm between the shoulder and the elbow joints, there are interesting objective sensory disturbances. There is total tactile anesthesia over the anterior surface of the upper arm and in the axilla, also over a quadrilateral area covering the right scapula for about 2 cm., the upper border of which corresponds to the entire length of the trapezius muscle. Immediately above and below this area for 1.5 cm. there is hypo-esthesia which gradually blends with the normal skin. Pain and temperature senses are abolished in the anesthetic area. Deep sensibilities are also involved: pressure sense is diminished in the affected areas; there is, in addition, inability to recognize objects placed on or pressed against the arm as well as the material of which the objects are made; for example, wood is taken for glass, or vice versa. Testing with the compass, gross errors are revealed not only over the anesthetic areas but also over the external and posterior aspects of the arm; when two points are separated at a distance of 8 cm. the patient recognizes them as one point.

The motor apparatus is involved in the entire limb; the grip of the hand is exceedingly weak; flexion and extension of the arm, forearm and wrist and all other voluntary movements are sluggish and can be easily overcome. The musculature of the entire limb is flabby, but there is no localized atrophy. Reflexes, station, gait, sphincters and pupillary reactions are all normal. The Wassermann reaction of the blood is negative.

Comment.—The sensory disorder presents some difficulty in localization: 1. In cerebral anesthesia, generally speaking, the deep sensations are usually and especially involved—the muscular sense, localization, tactile discrimination and stereognostic sense are affected. In such cases there is usually a certain amount of motor incoordination. 2. If this sensory syndrome is of cortical origin, the superficial sensations are as a rule intact. 3. In central or capsular hemianesthesia there is usually a more or less pronounced hemiplegia; the sensory disorder involves all forms of sensation and vision in particular, producing hemianopia. 4. In thalamic lesions we usually find a more or less pronounced hemianesthesia in the superficial sensations (touch, pain, temperature), but always very marked disturbance in the deep sensibilities. There are also pronounced subjective sensory disturbances of a dysesthetic nature. Finally there is a slight hemiparesis without contractures. 5. In peduncular, bulbar or pontile lesions, the hemianesthesia is frequently of a syringomyelic character, and the accompanying hemiplegia is quite pronounced. 6. In cord disorders the sensory disturbances are global because of transverse lesions, besides being usually bilateral. 7. The sensory disturbances due to a lesion of the spinal roots are usually longitudinal and parallel to the axis of the limb. In the present case the cutaneous area affected corresponds to the distribution

of the posterior branches of the spinal nerves between the fifth cervical and the first dorsal roots, but there is a decided want of parallelism between the sensory and motor manifestations. 8. In sensory disorders of peripheral origin there is almost always integrity of the deep sensibilities, while the superficial sensations alone are disturbed. The latter are frequently dissociated: diffuse touch, pain and extreme temperatures are abolished over a more limited area than the complex sensation (very light touch, appreciation of distances with the compass). Moreover, the superficial anesthesia occupies an area much smaller than the area of the distribution of the corresponding nerves. 9. Finally, the question of hysteria should come into consideration. In this, anesthesia is complete for all forms of sensations and does not correspond to any organic localization. It is always segmentary in character and perpendicular to the limb. There are usually other stigmas of the great neurosis.

Considering all these possibilities, this case probably presents an example of the thalamic syndrome. The nature of the lesion cannot be determined with approximate certainty unless the history of malignancy may favor the possibility of metastasis.

TONUS OF SMOOTH MUSCLE. DRS. S. D. LUDLUM and ELLICE MCDONALD.

In studying the psychoses, we have been investigating the tonus of smooth muscle by roentgenograms of the intestines and by blood pressure phenomena. Contraction of blood vessels usually accompanies relaxation of the intestinal canal, and relaxation of blood vessels accompanies a spastic condition of the intestinal muscle. These observations coincide with the phenomena of sympathetic innervation on the one hand and vagus on the other, so that what we observed in the smooth muscle must have been produced through the innervation and not directly on the muscle.

We were able to produce the sympathetic phenomena in patients by giving potassium salts and sodium salts, but calcium salts produced vagus results as, in a measure, did magnesium, so we have reason to think that the salt balance in the blood is one of the important factors concerned with innervation and smooth muscle tonus.

From the work of the biologists, it has been determined that the action of the salts on tissue is as the concentration of the hydrogen ions (p_H) in the solution. Therefore, the degree of contraction or relaxation of smooth muscle should have a direct relation to the p_H of the blood serum.

We have shown in examination of about 200 cases by roentgen ray and blood pressure that there is a direct correspondence between the smooth muscle tone and hydrogen ion concentration in blood serum. Using the colon as visualized with the roentgen ray as the best index, we have constructed a scale, whereby the degree of tonus is an index hydrogen ion concentration and salt balance in the blood, and we contend that this constitutes a smooth muscle reaction. This reaction, combined with the speed of peristalsis and other physiologic data, gives an important insight into the physiology accompanying mental disorders.

It is interesting that the chemistry of the biologists can be introduced into general physiology which obeys the laws of chemistry, and that general medicine is rapidly coming to realize this, and that mental disorders are to be approached in the same way.

STUDY OF A FAMILY WITH FRIEDREICH'S ATAXIA AND SPINA BIFIDA OCCULTA. DR. T. H. WEISENBURG.

This paper will be published in full elsewhere.

Book Reviews

A Textbook of Psychology for Nurses. By Maude B. Muse, R.N., A.M., Instructor in Nursing Education at Teachers College, Columbia University, New York. Price, $2.50. Pp. 351. Illustrated. Philadelphia and London: W. B. Saunders Company, 1925.

Ever since the war, psychology not only has made inroads in the courses given in colleges but is also being used as a method of selection in entrance examinations to schools. Psychologists have been added to the staffs of advertising agencies, and now nurses are asked to consider the psychology of their patients. From the practical point of view the better educated a nurse is the more useful she becomes, but the difficulty is that all hospitals have a hard time in filling their training schools, and that the entrance requirements are gradually being diminished, so much so that some hospitals are willing to take in young women who have a bare knowledge of reading and writing. It is easier to make money in business so why take up a profession in which it is necessary to spend three years in preparation? In fact a great many hospitals have cut down the time from three to two years.

With the material, therefore, in hand, it is questionable whether psychology can be successfully taught, and secondly, whether the student nurses can apprehend what is being taught them, but if such be the case this is an excellent textbook for the purpose, for it is written by one who has had practical training as a nurse and a teacher.

The book is well prepared and is eminently practical, and each chapter has a summary, questions and answers and bibliography, so that it can be used as a textbook as well as a reference book.

Études Neurologiques. Second Series. By Georges Guillain. Price, 26 francs. Pp. 360. Paris: Masson & Cie, 1925.

In 1922 Professor Guillain published a volume of reprints of his own work and that of members of his staff. This was received with such favor that a second series has just been issued. The material is divided into eight parts and contains altogether forty papers. The first part is concerned with semiology of the nervous system; the second with the pathology of encephalitis; the third with the pathology of spinal cord diseases; the fourth with multiple sclerosis; the fifth with secondary degenerations; the sixth with the spinal fluid and meningitis; the seventh with parkinsonism, and the eighth with various contributions.

It is rather difficult to comment on the particular merits of any one contribution. These articles, however, promise well for the work to be expected from the successor of Prof. Pierre Marie..

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